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AMERICAN JOURNAL OF OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

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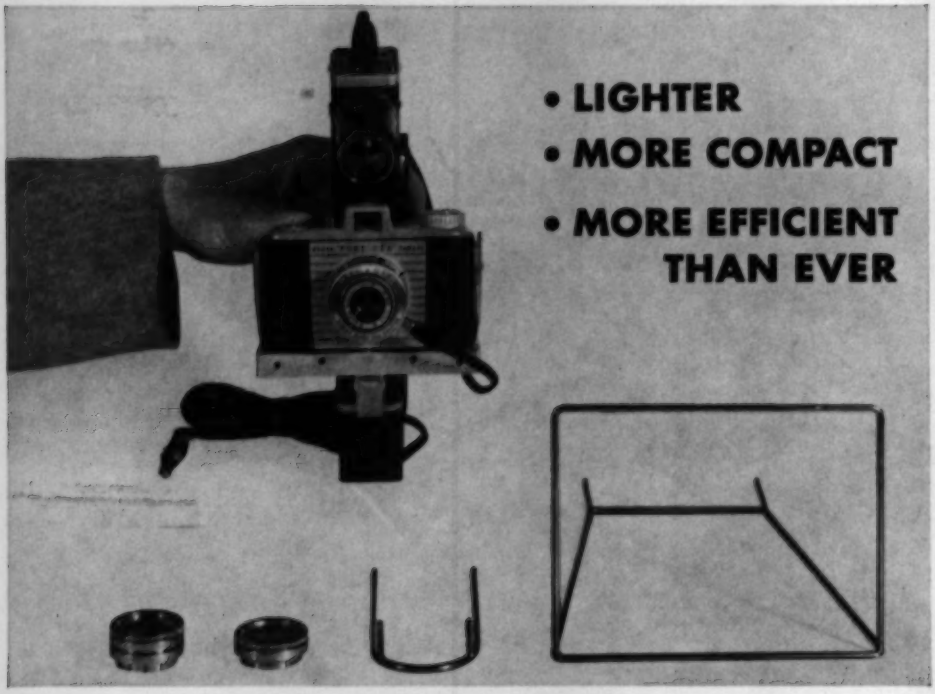

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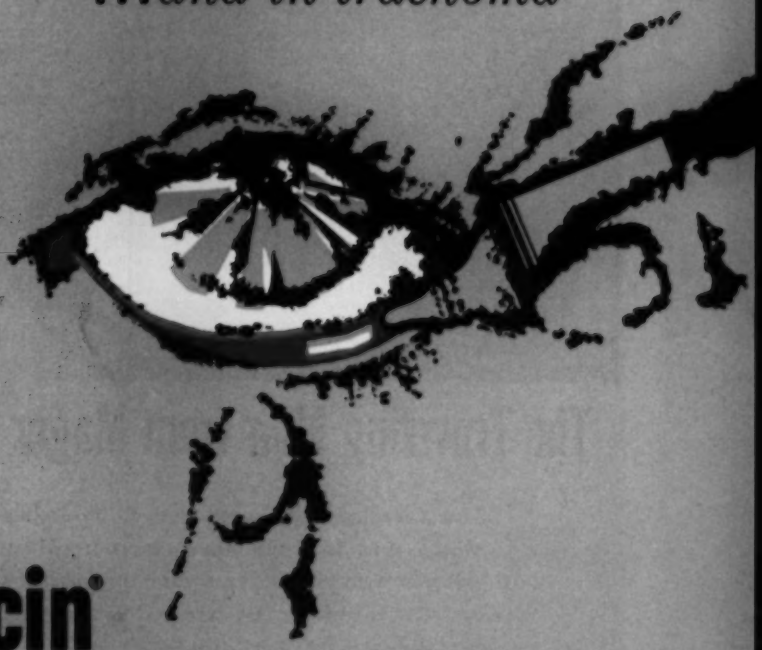

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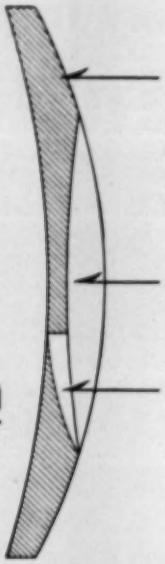
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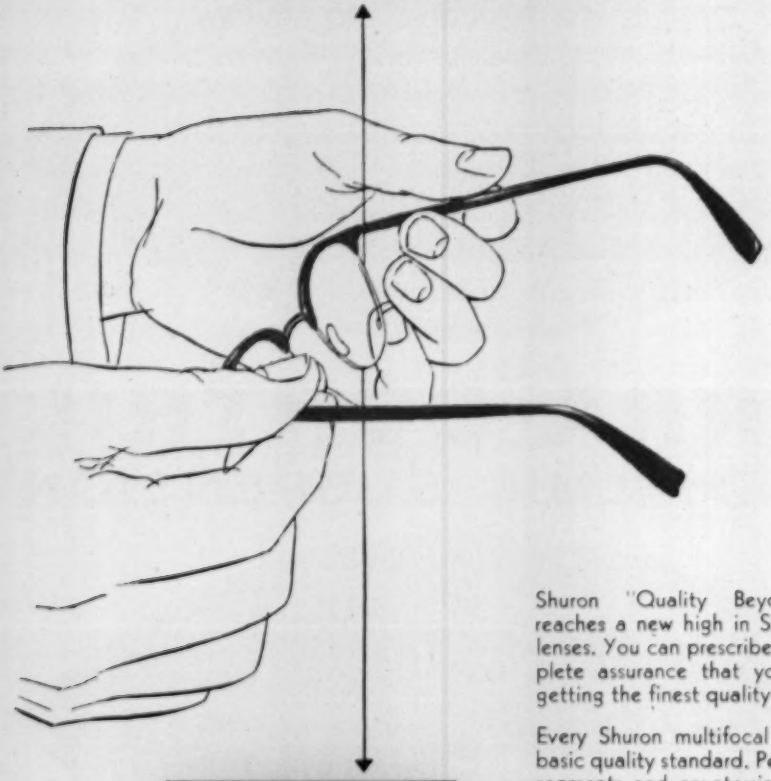

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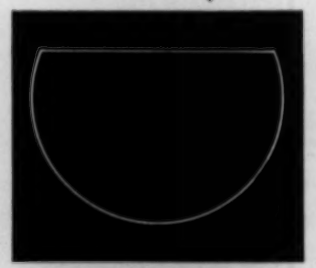

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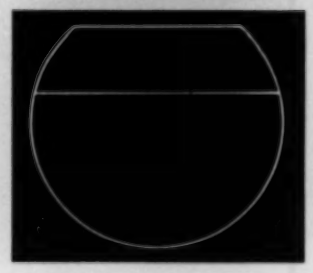

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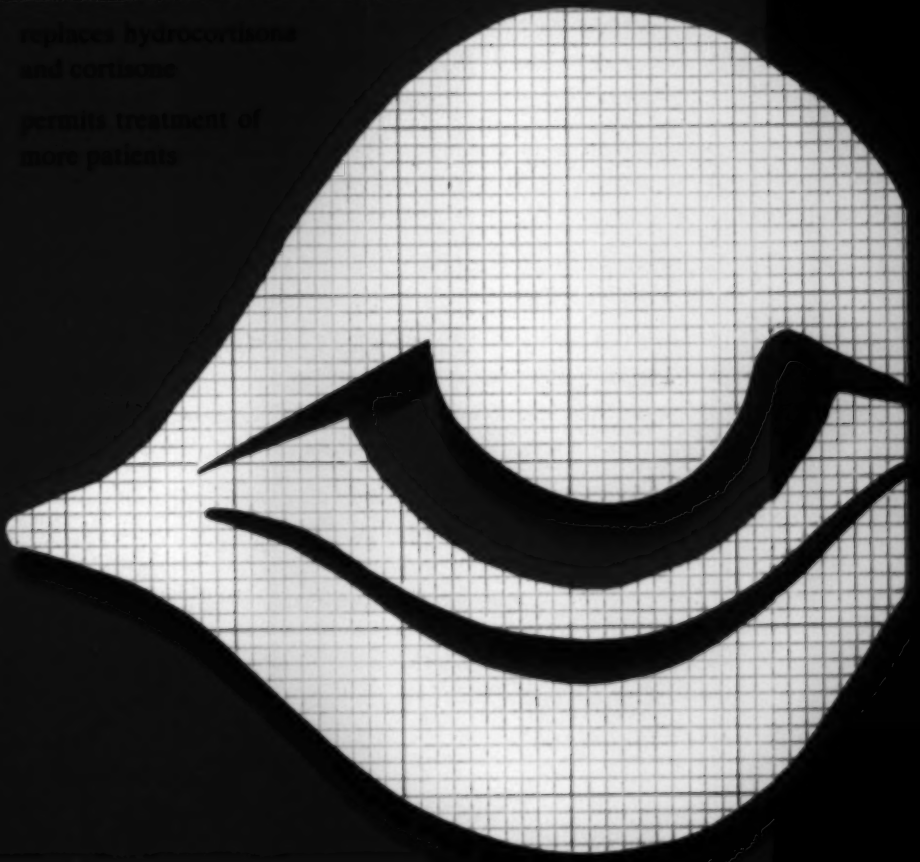

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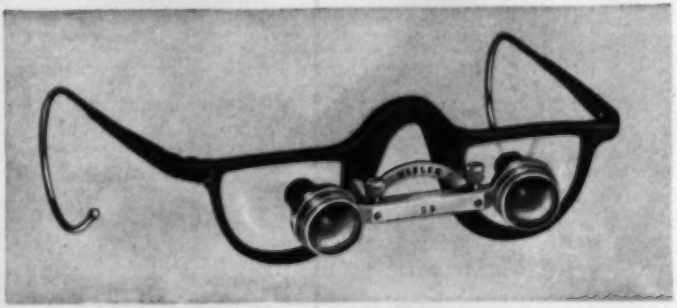

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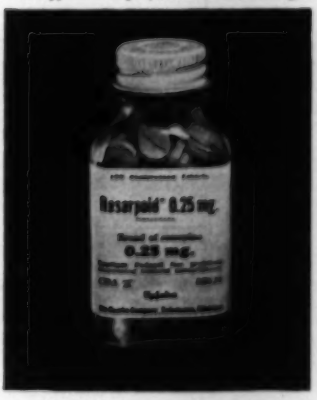

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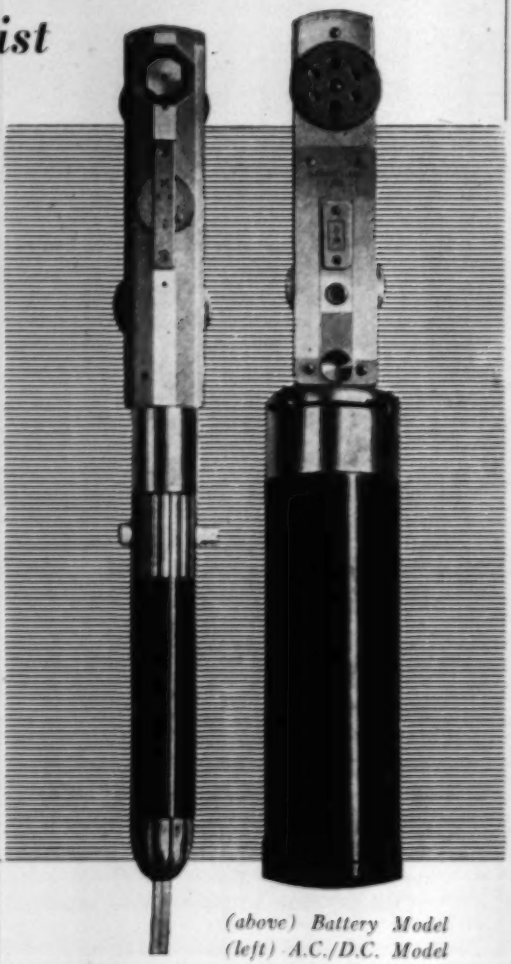

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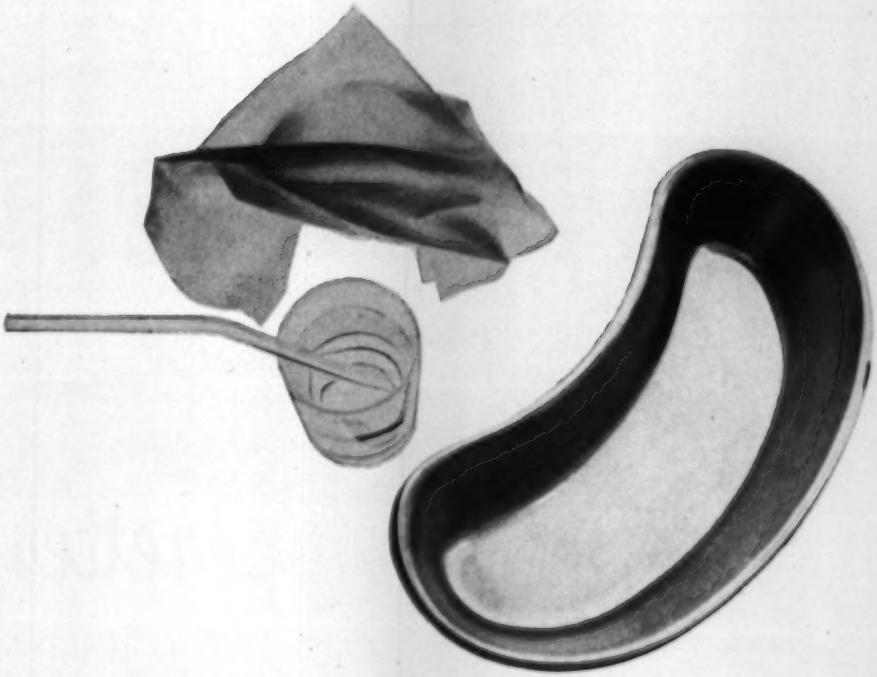

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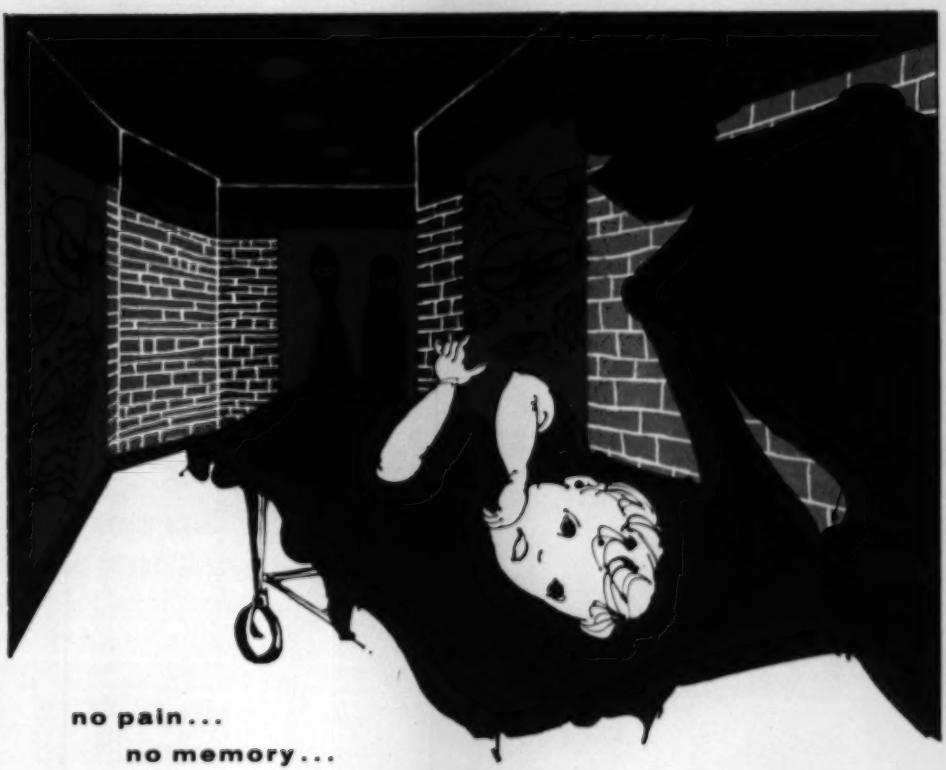

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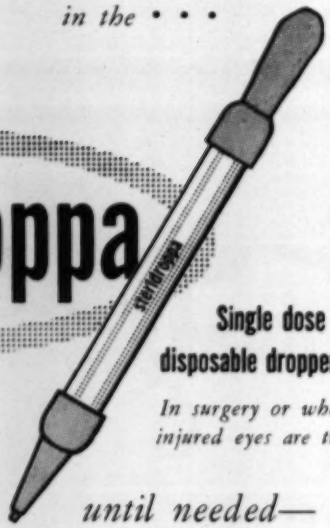

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Reference: 1. Hogan, M. J., Thygeson, P. and Kimuras, J., *Arch. Ophth.* **53**:165, Feb. 1955.

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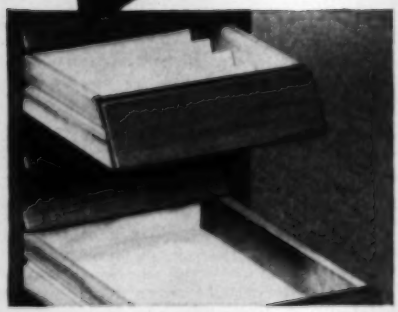

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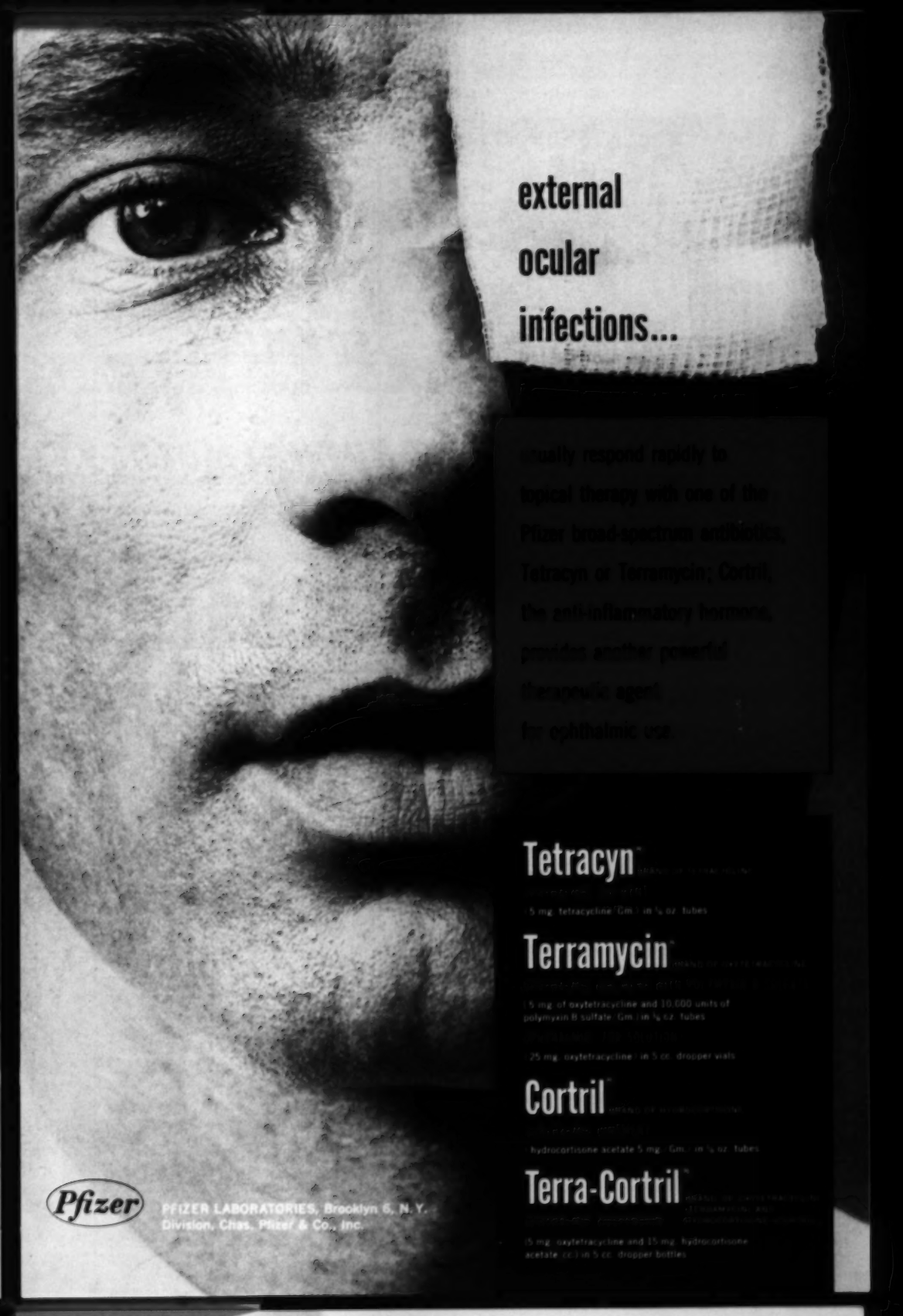
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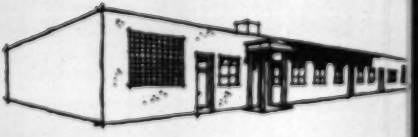

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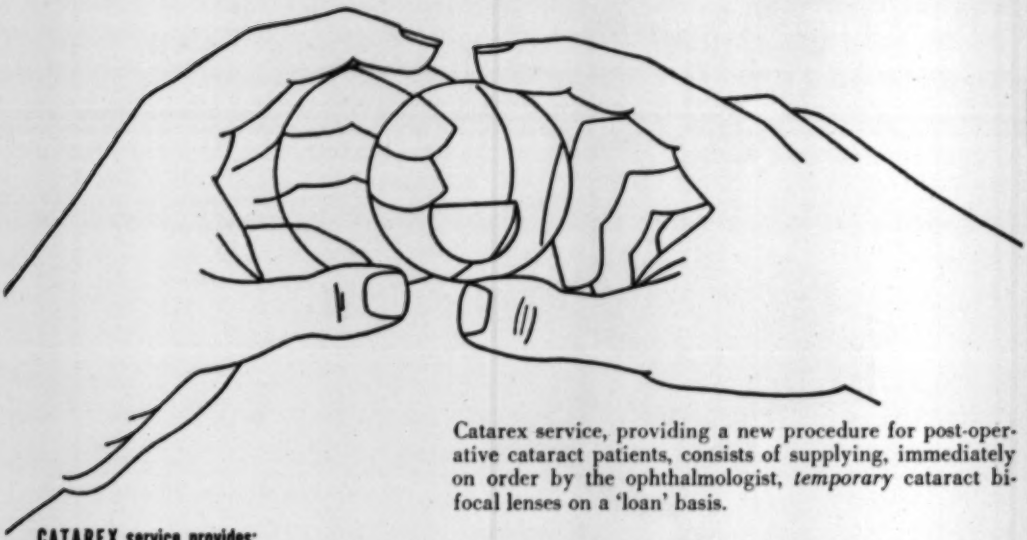

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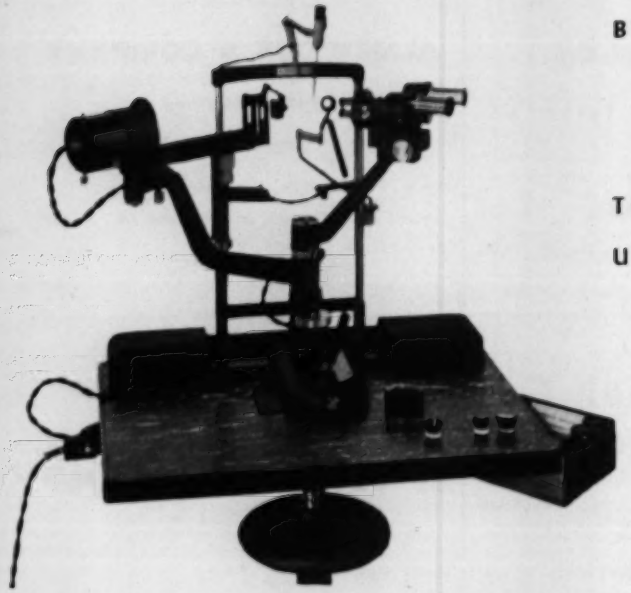

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ABSTRACTS

Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Neuro-ophthalmology; Eyeball, orbit, sinuses; Eyelids, lacrimal apparatus; Tumors; Injuries; Systemic disease and parasites; Congenital deformities, heredity; Hygiene, sociology, education, and history 724

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VOLUME 41 APRIL, 1956 NUMBER 4

PREDNISONE AND PREDNISOLONE IN OCULAR DISEASE*

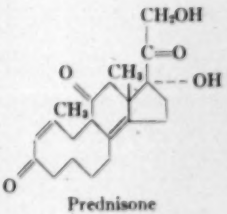
DAN M. GORDON, M.D.
New York

The introduction of cortisone and hydrocortisone with their attendant success in ocular therapy has inevitably sparked a search for better analogs of these steroids. The chief aim of these investigations is the development of a compound that has the maximal curative power and minimal ability to produce undesirable side effects. A host of compounds has been produced during this hunt. The latest are the delta[1, 2] compounds of cortisone and hydrocortisone, prednisone and prednisolone, respectively. At the time of introduction, their clinical use was said to be comparatively free of the undesirable side effects produced by cortisone and hydrocortisone.[1] In addition to rheumatoid arthritis and allied conditions,[1-3] these new steroids have proved to be of value in bronchial asthma,[4-6] the adrenogenital syndrome,[7] pemphigus vulgaris,[8] and various dermatoses[9] and ophthalmologic conditions.[10]

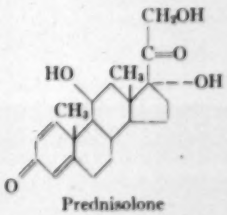
A total of 87 patients is reported here, 29 treated with systemic, or combined systemic and topical, therapy and 58 with topical alone.

CHEMISTRY

Prednisone ($\Delta^{1,4}$-pregnadiene-17α,21-diol-3,11,20-trione) and prednisolone ($\Delta^{1,4}$-pregnadiene-11β,17α,21-triol-3,20-dione) are synthetic derivatives of cortisone and hydrocortisone[11] with the following structural formulas:



Prednisone



Prednisolone

They are produced by dehydrogenation of the cortisone and hydrocortisone nuclei at positions 1 and 2. They possess a high degree of corticoid activity, approximately three to four times that of cortisone and hydrocortisone. Sodium retention and potassium depletion are said to be unlikely with prednisone and prednisolone.[1-9] There is, consequently, a striking quantitative difference in the excretion of these substances as compared with that under the influence of cortisone and hydrocortisone, although the excretion patterns are similar.

CLINICAL EVALUATION

Prednisone and prednisolone have been used in a large number of patients in order to evaluate them clinically, and to compare

* From the Department of Surgery (Ophthalmology), New York Hospital, Cornell University Medical Center. The prednisone and prednisolone used in this study were supplied by Harry V. Pifer, M.D., Schering Corporation, Bloomfield, New Jersey, and Elmer Alper, M.D., Merck & Co., Rahway, New Jersey, and Avery Cotton, M.D., Upjohn Company, Kalamazoo, Michigan.

the results with those of previous therapy using cortisone, hydrocortisone, 9-alpha-fluorohydrocortisone, and corticotropin. The results are presented only for those patients on whom sufficient informative data have been gathered.

Topical therapy

Prednisone and prednisolone have been employed topically in ophthalmic suspension and ointment forms. Prednisone acetate and prednisolone free alcohol were available in ophthalmic suspensions of 0.125- to 1.0-percent concentrations. All forms proved clinically effective.

The 0.25-percent suspension was considered optimal. No additional benefits accrued from the use of 0.5- or 1.0-percent prednisone or prednisolone suspensions. In turn, the 0.25-percent suspensions were little more effective than 0.1-percent. Prednisone acetate and prednisolone free alcohol appeared to be equally effective in equivalent concentrations. The latter was slightly more irritating locally, although not to an appreciable extent.

The acetate and alcohol forms of compounds were utilized in ointments of 0.1- to 0.5-percent strength. The 0.5-percent strength appeared to be optimal. It was difficult to judge which of the four compounds was the most effective. However, the prednisolone alcohol in 0.5-percent concentration seemed to be the best of the preparations employed.

During the early course of this work, the ophthalmic suspensions were prepared extemporaneously using saline as the diluent. No claims for elegance are made for these preparations. It is quite probable that the occurrence of irritation (most of these claims were not volunteered, but elicited by the examiner) would be minimized or eliminated by better pharmaceutical compounding.

In an attempt specifically to evaluate the steroid itself, mydriatics and antibiotics were not employed except when synechias were present. Later work, not included in this report, indicates the value of adding antibiotics or sulfonamides* in the case of limbal ulcers, of certain instances of conjunctivitis, and where infection is thought to be the prime factor.

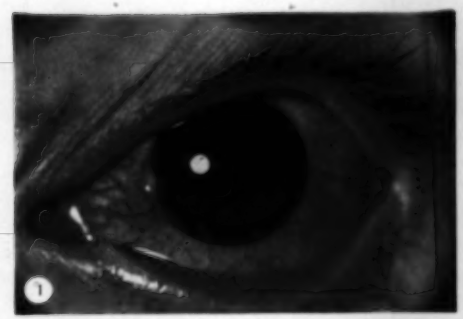
The successful treatment in 11 of 16 cases of anterior uveitis, using topical therapy without routine mydriatics, highlights the efficiency of the meti-compounds. Most of these 11 patients exhibited an excellent response within one or two days after beginning therapy and were sign and symp-

* Supplied by Schering Corporation as Metimyd.

Key to Figures 1–8

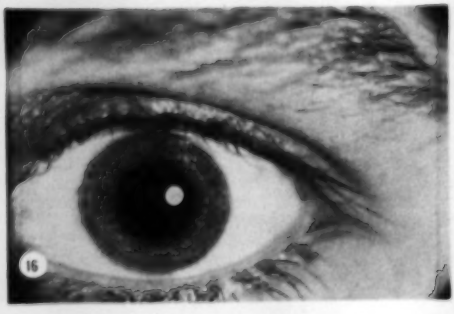
Figure No.	Patient	Diagnosis	Treatment	Before	After
1 and 2	G.	Episcleritis	Prednisolone (Topical)	Before	4 days after
3 and 4	H.*	Sympathetic ophthalmia	Prednisone (Topical and Systemic)	2 weeks after beginning treatment	6 days later; vision = 20/15
5 and 6	D.	Uveitis with hypopyon	Prednisone (Systemic)	Before	6 days after
7 and 8	A.†	Acute hypopyon uveitis with fibrin	Prednisone (Topical and Systemic)	Before	13 days later; vision = 20/15. Note round pupil. Phemylephrine (10%) was used for 4 days. No atropine used.

* Seen in consultation with Dr. Isadore Givner.
† Referred by Dr. L. Samuels.



Before treatment

After treatment



Before treatment

After treatment

tom free within five to seven days. In all cases, topical therapy was continued for an additional two weeks after complete disappearance of signs and symptoms. One drop of the suspension was instilled into the eye every two to three hours while ointment was instilled before retiring. Where vision was markedly reduced, the longer-acting ointment was substituted for the drops.

Three of the five failures showed an excellent response to systemic therapy with prednisone or prednisolone. A fourth has done poorly on hydrocortisone and corticotropin as well, after initially doing very well on combined systemic and topical therapy with the prednisone and prednisolone. The fifth patient responded well to prednisone systemically. She complained of palpitation, insomnia, and weight gain. Later, she suffered a relapse and refused to continue systemic therapy because of palpitation. Topical therapy alone proved insufficient. This patient was then placed on hydrocortisone but discontinued it for the same reasons that motivated refusal of prednisone. Two weeks ago, prednisone therapy with phenobarital to control the palpitation was reinitiated. The patient is now exhibiting marked improvement and is free of the palpitation. This patient is pregnant. The systemic therapy has in no way interfered with her status.

One patient with severe nonspecific keratitis of more than one month's duration improved during the application of 0.5-percent prednisolone alcohol ointment for two weeks and then suddenly exhibited a dendritic pattern on the cornea. This was satisfactorily treated with iodine cautery and antibiotic ointments. The marked improvement in the corneal folds, and so forth that had been produced by prednisolone markedly shortened the course of therapy. This patient had been treated elsewhere with iodine cautery and antibiotics during the month preceding the prednisolone and the condition had grown steadily worse. The steroid was discontinued when the dendritic keratitis appeared. (It was later learned that this man had had a dendritic ulcer two months earlier.)

All of the cases of conjunctivitis treated were severe. Each improved without the use of antibiotics. In one instance, an excellent response to prednisone alone occurred despite a four-plus culture of pneumococcus. This concurs with my thought that most cases of conjunctivitis that exhibit positive cultures may represent allergic responses to the organisms rather than true infections, and hence would be responsive to steroid therapy, as most of these cases do in my experience.

In general, prednisone and prednisolone appeared to be more effective than cortisone, or hydrocortisone in the same conditions.

Subconjunctival injections were employed

KEY TO FIGURES 9–16

Figure No.	Patient	Diagnosis	Treatment	Before	After
9 and 10	O.	Fibrinous iridocyclitis	Prednisolone (Topical)	Before	8 days after
11 and 12	C.	Lid allergy	Prednisolone (Topical)	Before	9 days after
13 and 14	K.	Limbal ulcers	Prednisone (Topical)	Before	4 days after
15 and 16	T.	Iritis	Prednisone (Topical and Systemic)	Before	19 days after

TABLE 1

TOPICAL THERAPY

Diagnosis	Total Number of Patients	Prednisone Number of Patients	Prednisolone Number of Patients	Results	
				Successful	Failures and Comments
Anterior uveitis	16	7	9	11	Prednisone, 2; prednisolone, 2; both, 1
Allergy, local	9	6	3	8	Prednisolone, 1; "too irritating"
Conjunctivitis	13	9	4	12	Prednisolone, 1; "too irritating"
Postoperative reaction	5	1	4	5	Tearing, redness, discomfort reduced
Limbal ulcers	2	1	1	2	In 1, the addition of sodium sulfacetamide accelerated the response during a relapse
Vernal catarrh	3	2	1	3	In 2 cases response more dramatic than on hydrocortisone; in 1, same. In 1, addition of 5 mg. prednisone daily was beneficial; in the other, it made no difference
Episcleritis	1	1		1	
Corneal abrasion	2	2		2	No deterrent effect upon healing; marked relief of pain
Keratitis	2	1	1	1	1 patient with severe keratitis (etiology ?) did well for two weeks and then developed typical dendritic keratitis
Blepharitis	2	1	1	2	
Meibomitis	3	2	1	1	2 (one on each)

twice, with 5.0 mg. of prednisone acetate. No beneficial effects were noted. Absorption from the subconjunctival space appeared to take place rapidly, possibly too quickly for good therapeutic effect. This has also occurred with 9-alpha-fluorohydrocortisone. Of course, no conclusions can be drawn from experience in two patients.

Combined topical and systemic therapy is being evaluated in anterior uveitis in order to determine whether or not the use of the medication topically will permit a decrease in the systemic dosage when the latter is necessary. Prednisone and prednisolone systemically were effective in controlling intraocular inflammation, but they did not rapidly turn the red eye pale. The topical therapy performed this function effectively and simultaneously permitted a decrease of 5.0 to 10 mg. daily in the systemic dosage.

One patient, seen in consultation with Dr. Alice Erlanger, exhibited a severe optic neuritis and generalized uveitis. This patient did well on corticotropin in doses of 120 units, initially, but with poor response of the anterior chamber reaction. When topical prednisone was added, the anterior chamber beam and cells rapidly cleared.

SYSTEMIC THERAPY

Both prednisone and prednisolone were employed systemically, often with concomitant topical application of the same drug. Initially, doses as high as 80 mg. per day were utilized, with rapid decreases as the condition responded. Later, 40 mg. daily became the standard initial dosage in severe conditions and 30 mg. in less severe cases.

Fortunately, a large group of patients with chronic uveitis was available. These patients had been under treatment and observation for one to five or more years and their response to other steroid therapy was known. Using some of these as the basis for comparison, it would appear that, in ocular inflammation, prednisone and prednisolone are approximately two and a half to three times as effective as cortisone or hydrocortisone in the same dose. Therefore, the requirements of the meti-compounds are 30 to 40 percent of cortisone or hydrocortisone in similar circumstances.

TABLE 2

SYSTEMIC THERAPY

Patient	Diagnosis	Initial Dosage	Response (days)	Remission (days)	Result	Comments
1. B. C.	Allergy, chronic	Prednisolone* 30 mg.	1	8	Excellent	Cortisone and allergy workups and treatment unsuccessful
2. W. T.	Anterior uveitis, chronic	Prednisone* 30 mg.	4	14	Good‡	Lens removed successfully under therapy
3. G. L.	Uveitis, chronic, general	Prednisone* 40 mg.	3	21	Excellent	Now well controlled on 20 mg. daily
4. V. P.	Choroiditis	Prednisone 40 mg.	5	5	Good	Developed Cushing-like side effects, a on hydrocortisone and ACTH; weigh gain
5. E. M.	Uveitis, chronic (Boeck's)	Prednisone* 20 mg.	2	7‡	Good	Requires constant treatment
6. M. H.	Pemphigus vulgaris	Prednisone* 60 mg.	3		Good	Remission incomplete; good control
7. G. H.	Uveitis, chronic, general	Prednisone* 60 mg.	6		Good	Remission incomplete varies‡ to no anterior chamber reaction
8. F. G.	Choroiditis, recurring	Prednisone† 40 mg.	7	21	Excellent	No response to subconjunctival injection
9. S. B.	Vernal catarrh	Prednisone*	2		Good	Aided control by topical
10. M. K.	Vernal catarrh	Prednisone*	10		None	Well controlled by topical; systemic added nothing
11. M. T.	Iridocyclitis, acute	Prednisolone* 60 mg.	5	15	Excellent	Mydriatic employed for 1 day only
12. A. T.	Choroiditis, chronic	Prednisone 40 mg.	7		Good	Still under treatment; lesions clearing well
13. K. M.	Optic neuritis	Prednisolone 80 mg.			None	10 days treatment, no improvement. Excellent result on intravenous ACTH beginning on 3rd day
14. A. D.	Uveitis, recurring, general	Prednisone* 70 mg.	5	50	Excellent	Well maintained on 10 mg. daily
15. E. E.	Uveitis, chronic	Prednisolone* 40 mg.	4	12	Excellent	Treatment continues to prevent relapse
16. L. B.	Choroiditis, chronic	Prednisone 60 mg.	36		Good	Continues on therapy to prevent relapse
17. N. E.	Uveitis, recurring	Prednisone* 50 mg.	17	38	Very good	Cushinglike side effects; worse on cortisone with general body edema
18. D. G.	Iritis, acute	Prednisone* 40 mg.	6	14	Excellent	Palpitation, weight gain
19. J. K.	Post uveitis	Prednisone* 60 mg. Prednisolone* 60 mg.	10		Good, then poor	Initial excellent response then relapse, uncontrolled by prednisone, prednisolone, hydrocortisone, or ACTH
20. H. J.	Uveitis (Boeck's)	Prednisone* 60 mg.			Very good	Previously maintained on 80–100 mg. hydrocortisone. Under treatment over 5 years
21. D. R.	Uveitis, chronic general	Prednisone* 30 mg.			Excellent	Previously controlled by 50–60 mg. hydrocortisone
22. D. M.	Choroiditis, chronic	Prednisolone			Excellent	Previously controlled with 40 mg. hydrocortisone. Now on 15 mg. prednisolone, lesion hardening
23. M. M.	Central serous	Prednisolone 40 mg.	2		Excellent	Vision 20/15 after 2 weeks' therapy; edema cleared
24. A. R.	Pseudotumor exophthalmos	Prednisone			Good	Better control than with cortisone
25. J. D.	Choroiditis, acute	Prednisone 60 mg.			Poor	After 8 days given ACTH, required 120 units for good result
26. H. K.	Uveitis, chronic	Prednisone* 40 mg.	7		Excellent	Requires constant medication for control
27. A. D.	Recurrent uveitis	Prednisone* 40 mg.	2	13	Excellent	
28. E. B.	Allergy	Prednisone 10 mg.	3 hr.	3 hr.	Excellent	No further systemic treatment
29. D. M.	Chronic macular choroiditis	Prednisolone 15 mg.		60 hr.	Excellent	Substituted for 30-40 mg. hydrocortisone

* Also topical treatment of same drug.
† Also one subconjunctival injection of 5.0 mg. prednisone.
‡ Still under treatment, controlled but remission not permanent.
NOTE: Since many of the chronic patients were already under control when switched to the meti-compounds, the date of response cannot be given. Where permanent control is needed, there is no remission.

Few dramatic results were noted, especially in view of previous experience with steroid therapy using corticotropin, cortisone, and hydrocortisone. The one failure in optic neuritis and King's[10] failures in the same disease parallel similar experiences with cortisone and hydrocortisone in optic-nerve inflammation. Givner[12] had an excellent result with 30 mg. prednisone daily, with improvement occurring on the third day of treatment. When prednisone was withdrawn in an attempt to determine whether or not the improvement had been spontaneous or represented a response to the steroid, a relapse occurred during which the patient could only distinguish hand movements.

Within four days after reinitiating prednisone therapy, the vision returned to 20/15.

At the time this paper was submitted for publication, a patient with sympathetic ophthalmia receiving prednisone systemically, on a dosage schedule of 40 mg. per day, quickly responded to therapy. Vision changed in the sympathizing eye from 20/200 to 20/15 within 10 days.

A physician with a central serous retinopathy of over three weeks' duration and who exhibited a large central scotoma has made an excellent response to prednisone therapy. Starting initially with 40 mg. per day, rapid improvement was made and vision was returned to 20/15 with loss of the scotoma.

A patient with orbital pseudotumor and marked exophthalmos, who was being treated with 100 mg. cortisone daily by Dr. Frank B. Walsh, was seen in consultation and placed on 30 mg. prednisone daily. Dr. Walsh reports that the response to prednisone is much better than to cortisone.

The metabolic effects of prednisone and prednisolone are similar to their parent compounds, cortisone and hydrocortisone.[13-15] Four patients exhibited manifestations similar to those in Cushing's syndrome (moon-face, and so forth). Two had marked weight gain, which they also had on other steroid therapy. One patient, sensitive to cortisone and in whom the latter steroid caused generalized body edema, exhibited only a mild rounding of the face on prednisone. One patient with palpitation has already been mentioned. She also had a mild acneform eruption of the face, which disappeared with cessation of therapy and did not recur during her second course of oral therapy. One other patient, receiving 40 mg. prednisolone daily, developed mild acne during the second week of therapy.

Indications and contraindications

The indications for prednisone and prednisolone therapy are the same as those for other steroids—ocular inflammation, edema, and allergy. The contraindications also appear to be the same. Herpes simplex infection is the principal one of these. Herpes zoster is an indication. Prednisone and prednisolone merit trial in conditions where the other steroids and/or corticotropin have failed. Inevitably, some patients will fail to respond to one steroid and will be benefited by another. With the introduction of prednisone and prednisolone, two new compounds are available that may be of value in such situations.

Conclusions

Preliminary evaluation indicates that prednisone and prednisolone are clinically superior to cortisone and hydrocortisone when employed topically in the eye. Systemically, their effect in ocular conditions is much the same as that of cortisone and hydrocortisone but smaller dosages are required. The incidence of important side effects in our series of patients was not significantly less than with other steroids.

Addendum

Experiences since this paper was submitted for publication, with a series now several times that reported, confirms the efficiency of prednisone and prednisolone.

These are potent forms of steroid therapy; with the results obtained dependent upon an understanding of their application. Experiences now covering over six years reveal that there is still considerable misunderstanding and misapprehension concerning the basic rules governing the application of steroid therapy in ophthalmology.

The indications for the use of hormonal-steroid therapy are symptomatic—edema and inflammation, regardless of cause. The known contraindication is dendritic ulcer (herpes simplex) of the cornea. One must not confuse this with herpes zoster which is an indication. Topical therapy is indicated in all external conditions (those which can be seen with the naked eye) and in most cases of anterior uveitis (iridocyclitis). In

the latter condition, it is advisable to shorten the duration and intensity of the disease by the use of systemic hormonal-steroid therapy for the first several days of the acute process, on an ambulatory basis. Topical therapy is valueless when the disease process is located behind the ciliary body (posterior uveitis [choroiditis], optic neuritis). Here systemic use of the various compounds is mandatory if one is to achieve success. The use of steroids topically as the sole therapeutic agent in posterior intraocular inflammatory disease is evidence of ignorance of their action.

There is no such thing as a "course" of steroid therapy; the daily dose and duration of treatment are individual in each case and dependent upon the response of the patient. One must employ sufficient amounts initially to suppress the disease process; and then, once that response has been obtained, keep it suppressed, with gradually decreased doses, until the patient becomes completely sign and symptom free when off medication. An increase in symptomatology is a signal to increase the dose, a decrease in symptomatology signals a decrease in the amount given. In external disease, such as an eyelid allergy, topical therapy alone may be insufficient. The addition of 5.0 to 10 mg. daily in three or four divided doses may turn the tide.

The most common errors are the employment of topical therapy when parenteral is demanded; and the use of too small doses initially. Two cases will illustrate this:

A man with central serous retinopathy had been treated for three weeks with 20 mg. of Meticorten daily and remained unimproved with vision at 20/200, when first seen. When the dose was stepped up to 40 mg. daily, vision increased to 20/30 by the third day.

A second case, one of severe choroiditis, had been on 100 mg. of cortisone daily followed by 30 mg. of prednisone daily for a period of five weeks, prior to my examination. The dose was increased to 40 mg. for a week, without demonstrable effect. It was then increased to 60 mg., with marked improvement within several days.

The moral here is that, when one employs medication, enough of the drug should be used to produce the desired result. And it should be administered only by the route which offers hope of success.

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HUMAN TOXOPLASMOSIS*

With special reference to intraocular inflammation: A critical review

The Sixth William Hamlin Wilder Memorial Lecture

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I was highly honored by your invitation to give the Wilder Memorial Lecture on the subject of human toxoplasmosis. I accepted this invitation with reluctance because I have not worked in this field for the past six years. However, since this happens to be the 20th anniversary of my accidental introduction to studies on toxoplasmosis, I could not resist the temptation of the opportunity you offered me to review in a critical manner the interesting current dilemma regarding the nature, frequency, and identification of postnatally acquired and adult ocular toxoplasmosis.

Although *Toxoplasma gondii* was first reported as a new protozoon species in 1909, 30 years passed before definite proof was obtained of its role in human disease. During this early period of predominantly morphologic observations many organisms were called Toxoplasma which were not Toxoplasma, for example, certain protozoa of birds or even histoplasma, while others which we now have every reason to believe were Toxoplasma were not recognized as such and were called by a variety of other names. Thus Jankû, who was perhaps the first to see Toxoplasma in the human eye, in 1923 merely called the organisms Sporozoa. In subsequent years, Torres reported on *Encephalitozoon chagasi*, Coulon on *Encephalitozoon brumpti*, and as late as 1937 Wolf and Cowen reported on *Encephalitozoon hominis*. Progress was not made until the morphologic observations were supplemented by the recovery and preservation of the parasites by animal inoculation that permitted the biologic and immunologic comparisons which finally established the identity of the organisms called Toxoplasma of animal, avian, and human origin.[1]

Without attempting a full documented list of the *proved* natural occurrence of Toxoplasma, the following domestic animals and birds have been proved to be carriers: the dog, cat, wild rat, pig, sheep, goats, cattle, rabbits, guinea-pigs, pigeons, and chickens. The importance of these various potential sources of Toxoplasma for infection of human beings may vary under different circumstances and is difficult to assess, but the recent studies of Cole and his associates[2] in Ohio have established beyond doubt an association between Toxoplasma-shedding, chronically infected dogs and the occurrence of proved human infections. It is particu-

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larly noteworthy that chronically infected dogs, and undoubtedly other animals, with demonstrable antibody in their serum, can for many weeks continue to shed Toxoplasma in their feces, derived from intestinal ulcers, or in their respiratory secretions derived from lesions in the lungs and elsewhere in the respiratory tree. In 1941, Dr. Warren and I[1] demonstrated Toxoplasma in the urine obtained by bladder puncture in an experimentally infected young dog. Although many studies have been carried out on arthropods, it has not yet been possible to show that they can transmit infection by biting. Thus, there has gradually accumulated a well-documented body of knowledge which permits the conclusion that the protozoon parasite originally recovered from the North African rodent, the gondi, and described as *Toxoplasma gondii,* is present in almost all parts of the world, and by a variety of means is naturally transmitted among many animals and certain birds, and seemingly also to hundreds of millions of human beings.

Our knowledge of human toxoplasmosis has been developing in a stepwise fashion since 1939. At first, it appeared that there were only rare fatal cases, both congenitally and postnatally acquired, because recovery and identification of the parasite was the only means at our disposal for proving that a given clinical condition was caused by Toxoplasma. To be sure, the apparent well-being of the mothers of the few proved cases of congenital toxoplasmosis very early suggested that inapparent or mild forms of the infection must occur in human beings. It was the development of serologic and immunologic methods—at first cumbersome, qualitative, and impractical, but with the discovery of the dye test[2] in 1948 much simpler and more widely applicable—that led to the demonstration of the extremely high incidence of Toxoplasma infection throughout the world. The demonstration at about the same time that a specific allergic state develops in most inapparently infected individuals, provided another tool in the form of a skin test[4-6] which could be applied like the tuberculin test in estimating the incidence of unrecognized and subclinical infection in large population groups. Largely as a result of the introduction of these methods, publications by the hundreds have emanated from all over the world since 1949—there are now more than 1,500 references on this subject. Just as the introduction of the tuberculin test and the Wassermann test led to innumerable communications in which attempts were made to associate clinically ill-defined syndromes or manifestations with tuberculosis or syphilis, so in recent years history has repeated itself in the case of toxoplasmosis.

A primary infection with Toxoplasma is characterized by a rapid rise in dye test antibody within one to two weeks to levels which are not less than 1:256 and can be as high as 1:32,000 or more. Tests for complement-fixing (C-F) antibody[7] are characteristically negative during the first weeks after infection and then rise to levels of 1:16 to 1:256. Both types of antibody can persist in high titers for several years, but while the C-F antibody then disappears completely the dye test antibody falls more slowly and with conceivable exceptions persists for life. Thus a high level of dye test antibody associated with a negative C-F test indicates either an acute infection of relatively recent onset, in which case the C-F test becomes positive in increasing titers during the forthcoming weeks, or that infection occurred not more than a few years ago, in which case subsequent C-F tests remain negative. After a few years the dye test titers drop to 1:64 or less, and in human beings there is every reason to believe that even the lowest titers are indicative of past infection with Toxoplasma. Physicians most frequently ask: what titers of Toxoplasma antibody are significant? The answer is that all titers are significant and that various titers and combinations of dye test and C-F antibodies can be interpreted in the manner set forth above.

An observation which I made on a patient in 1948 leads me to believe that high titers of dye test and C-F antibody may occasionally result also from a subclinical reactivation of a latent infection. In 1947 Feldman and I studied an epidemic of pneumonitis in a group of men who were exposed to pigeon excreta, which subsequently was proved to be caused by *Histoplasma capsulatum*. Extensive tests on this group of men showed no evidence of recent infection with Toxoplasma. However, one of these men with a very severe pneumonitis who had a very prompt antibody response to *Histoplasma capsulatum*, also exhibited a dye test titer of 1:16 and a negative C-F test for Toxoplasma shortly after the onset of his illness and also two months later. However, sometime during the course of the subsequent three months his Toxoplasma antibody spontaneously increased so that at five months after onset of his severe pneumonitis, he had a dye test titer of 1:1,024 and a C-F titer of 1:32 which persisted for at least a year. All this happened without any associated clinical manifestations of disease. This is not the picture of an anamnestic reaction because it occurred when his antibody response to *Histoplasma capsulatum* was falling rather than rising. Furthermore, none of the other patients in this epidemic showed any development or change in level of Toxoplasma antibody. It is conceivable that in this particular patient rupture of latent pseudocysts in the lungs, lymph nodes, or other viscera may have supplied the stimulus for the boost in Toxoplasma antibody.

It is not yet known how soon the allergic state develops after a primary infection with Toxoplasma. It is known, however, that children with unequivocal evidence of congenital toxoplasmosis can give negative skin reactions, and that a varying proportion of adults who have antibody for Toxoplasma also give negative skin reactions.[6] However, the specificity of the skin test is so great that, with properly prepared and controlled antigen, positive tests are, with perhaps rare exceptions, obtained only in individuals with serologic evidence of past infection with Toxoplasma. The skin test has, therefore, been a very useful tool for estimating the incidence of unrecognized and subclinical toxoplasmosis in many different parts of the world. Feldman and I[8] first demonstrated that the incidence of positive skin tests in "normal" individuals in Cincinnati rose progressively from five percent in the five- to nine-year group to 50 percent in the fourth decade, to 65 percent in those aged 40 years and over. Thalhammer[5] recently reported on 1,647 dye tests and 1,006 skin tests on "normal" individuals of different ages in Vienna and, in addition to obtaining a remarkable parallelism between the two tests, found the same rising age incidence as in Cincinnati except that in Vienna the 60 percent level was reached as early as 21 years of age. Feldman[9] reported a similar more rapid rise in incidence in Syracuse, and his extensive studies on populations in different parts of the world range all the way from completely negative results among Eskimos in Alaska to an average incidence of 70 percent for all age groups in Tahiti. It is this great variation in the incidence of subclinical infections among different age groups and different populations of different regions that renders the statistical approach so difficult and unreliable in any attempt to correlate Toxoplasma infection with certain syndromes of undetermined but nevertheless multiple potential etiology.

It is not an unreasonable estimate that hundreds of cases of congenital toxoplasmosis have now been diagnosed in all parts of the world—the vast majority in surviving children of different ages.[9,10] The combination of clinical manifestations, of which chorioretinitis is the most frequent, that have been established in proved fatal cases of the congenital disease together with the invariably high titers of antibody in the mother and affected child have formed a solid basis for diagnosis. The accumulated observations strongly suggest that when the infection is

transmitted to the fetus early in pregnancy the nervous system, including the eyes, bears the brunt of the attack. Infection transmitted toward the end of pregnancy affects the nervous system and eyes less and the viscera more giving rise to the now well-recognized combination of rash, jaundice, and hepatosplenomegaly. In postnatally acquired infections, even in those manifesting themselves predominantly as an encephalitis, there has until recently been no clinical evidence of an associated chorioretinitis.

In 1952, Wising[11] was the first to supply definite proof of the appearance of an acute chorioretinitis immediately after an acute febrile illness with generalized lymphadenopathy in a 31-year-old woman. The proof consisted of the demonstration of the typical marked rise in dye test antibody and the delayed subsequent rise in complement-fixing antibody which is the characteristic serologic pattern of infections of recent onset. A number of other communications, notably those of Magnusson,[12] of Hogan, Thygeson, and Kimura,[13] of Prior et al.,[14] of Rieger,[15] and of Woods et al.,[16] all contained case reports of recently acquired ocular infections in adults associated with high and even rising titers of dye test antibody. That this, however, is a rare complication of even the benign form of acquired toxoplasmosis characterized chiefly by lymphadenopathy, which has been studied most extensively by Siim[17] of Copenhagen, is evident from a personal communication that I just received from Siim. He wrote that ocular involvement was observed in only one of about a hundred patients with confirmed postnatally acquired toxoplasmosis.

The possibility that at least some of the many patients with active chorioretinitis of unknown etiology seen by ophthalmologists may be caused by Toxoplasma was suspected as soon as chorioretinitis was proved to be an almost constant feature of congenital toxoplasmosis. I must confess to being the first to attempt to establish "guilt by association" when I reported in 1942 that nine of 10 older children and adults with chorioretinitis of unknown etiology gave positive neutralization tests with Toxoplasma, while the incidence of such positive tests was only 10 percent in an unselected group of other individuals of various ages.[18] In 1943, Vail and his associates[19] reported on some of the patients that I had tested, and many subsequent reports appeared in which the incidence of Toxoplasma antibodies or skin tests was found to be higher among individuals with undiagnosable chorioretinitis. When the dye test and skin test surveys of normal populations pointed up the importance of age and locale, and when it became evident that millions of people had Toxoplasma antibodies without chorioretinitis while 50 percent or more of patients with suspect types of chorioretinitis yielded negative tests (Feldman recently informed me that he found only 38 percent positive among 339 patients tested), it became clear that the "guilt by association" statistical approach was most unsatisfactory. Serologic studies on individual patients were most unrewarding because with the few exceptions, mentioned earlier, the patients who did possess Toxoplasma antibody exhibited the low dye test titers and negative C-F tests that are characteristic of infections in the distant past.[10]

When the existence of an allergic state in human toxoplasmosis was first recognized, Frenkel[20] suggested that chorioretinitis in adults may represent an allergic inflammatory response to ruptured pseudocysts which may have been dormant for many years rather than to an acute primary infection of the eye. Proof of this hypothesis was difficult to obtain, and early in 1952 a special U. S. Public Health Service Committee, of which I was a member, unanimously agreed that "there is as yet no evidence that Toxoplasma is the cause of postnatally acquired chorioretinitis or other forms of uveitis."[10] This was before Wising's[11] definitive proof in a single case and the subsequent suggestive reports in a small number of other cases. To be sure, Wilder[21] had just reported her most

interesting finding of Toxoplasmalike structures in sections of enucleated, adult human eyes with granulomatous uveitis—but the consensus was that past experience with strictly morphologic identifications warranted a reservation of judgment until biologic confirmation could be obtained. This confirmation has now been supplied by Jacobs and his associates[22] by the recovery and unequivocal identification of *Toxoplasma gondii* from the enucleated eye of a 30-year-old man who exhibited the same type of granulomatous uveitis and Toxoplasmalike structures described by Wilder. Furthermore, the serologic studies on this patient as well as on 21 of the patients originally described by Wilder, in my opinion, justify the conclusion that an active granulomatous chorioretinitis may occur as a delayed and recurrent manifestation of Toxoplasma infections acquired even in the distant past—both congenitally and postnatally. The fact that all 21 of Wilder's group of 53 patients who could be rounded up for tests were found to have Toxoplasma antibody greatly exceeds the mere chance of random association.[23] The fact that with only three exceptions, these patients exhibited the low dye test titers and negative C-F tests indicative of infections in the distant past, must be taken as evidence that Toxoplasma may survive in some human eyes for many years and under as yet unknown conditions set up local inflammatory reactions which in most instances fail to boost the level of antibody. Although most of the patients were tested several years after enucleation, there were five patients with low titers whose eyes were enucleated a few months to one year before the serologic tests. The question naturally arises whether it is possible that not all Toxoplasma are antigenically alike and whether low titers obtained in tests with a single strain might reflect antigenic heterogeneity rather than infection in the distant past. Against this possibility are two facts: first, many strains have been compared (Siim[17]) without finding such antigenic heterogeneity and second, the serum of the patient from whose eye Jacobs et al.[22] recovered Toxoplasma had the same low dye test titer of 1:64 against his own strain as against the standard RH strain.

The possibility that congenitally acquired Toxoplasma may be the cause of ocular inflammation in adult life is suggested by the fact that among the 21 serologically tested patients with Toxoplasma in their enucleated eyes there were two, aged 29 and 41 years, with cerebral calcification. In this connection it is also noteworthy that the 40-year-old patient, with serologic evidence of toxoplasmosis, in whose eye Duke-Elder et al.[24] demonstrated Toxoplasmalike organisms, gave a history of defective vision "as long as he could remember." Also Woods et al.[16] observed older patients, one 65 years of age, with histories suggestive of probable congenital infection. Actual evidence that Toxoplasma pseudocysts can persist in the brain in a viable state for at least three years after a congenital infection was recently obtained by Dr. Georges Desmonts of Paris, when he recovered Toxoplasma by subinoculation in mice and after a careful search through 30 sections found a single characteristic pseudocyst (personal communication—photograph of pseudocyst shown).

All of these observations, taken together, provide strong support for Frenkel's hypothesis that adult ocular toxoplasmosis may represent an allergic inflammatory response to ruptured pseudocysts. The histologic picture described by Wilder is in keeping with this hypothesis, and differs in many respects from the predominantly acute necrotic chorioretinitis with abundant intracellular as well as extracellular Toxoplasma seen in the eyes of fatal congenital cases. For the sake of future studies on chemotherapy it would be important to know how often the Toxoplasma liberated from the pseudocysts remain scattered without being able to invade and multiply in new cells—for Toxoplasma are obligate intracellular parasites which do not multiply except within susceptible cells.

A careful microscopic review of Wilder's material and comparison with the lesions in acute fatal congenital cases should provide valuable information on this point. For if the chorioretinitis of adults is predominantly allergic without multiplication of Toxoplasma in new cells, one would expect no effect from using drugs like the sulfonamides, sulfones, and daraprim which inhibit multiplication of the organisms. On the other hand, the judicial study of the antiphlogistic corticoids, alone and in combination with the above drugs, would appear to be reasonable—the main difficulty, of course, being in the clinical identification of the cases that are of toxoplasmic etiology.

In the rare instances, in which a granulomatous posterior uveitis is associated with dye test titers of 1:256 or higher, particularly together with positive C-F tests, even when no changes in pattern suggestive of very recent infection are present, a presumptive diagnosis of toxoplasmosis would carry with it a very high probability of being correct. Since such high titers are only rarely encountered in the normal population and since granulomatous uveitis is by itself also a relatively rare manifestation, the product of the probabilities enormously increases the likelihood of an actual association between Toxoplasma and this clinical condition. The fact that such high Toxoplasma antibody titers have been encountered in patients with chorioretinitis who also have histories of brucellosis or tuberculosis,[16] presents a problem in differential diagnosis but does not diminish the possibility of a toxoplasmic etiology since the other infections might have contributed to the rupture of pseudocysts. However, the serologic studies on the patients with Toxoplasma in their enucleated eyes indicate that the criterion of high titers would exclude most of the patients with toxoplasmic chorioretinitis. Yet for the sake of controlled therapeutic studies it would be helpful to carry out observations on at least three groups of patients exhibiting clinically similar types of posterior uveitis: (1) those with high Toxoplasma antibody titers, (2) those with dye test titers of 1:64 or less, and negative C-F tests, and (3) those with repeatedly negative serologic and skin tests for toxoplasmosis. This type of systematic study might yield valuable results if many patients with chorioretinitis of undetermined etiology could be referred to a few selected ophthalmologic centers with technical facilities for Toxoplasma investigations.

Since neither the statistical approach nor serologic studies of individual patients can give us a correct estimate of the proportion of undiagnosable chorioretinitis, that is of toxoplasmic etiology, it would appear highly worthwhile to determine the incidence of Toxoplasma in eyes with such markedly advanced granulomatous uveitis that they have to be enucleated because of pain and blindness. If ophthalmologists could arrange to have most such enucleations done in two or three centers, in which proper facilities would be available for the recovery and identification of Toxoplasma in the same manner in which it was done by Jacobs and his associates[22] on a single enucleated eye, much valuable information could soon be obtained. On the basis of past experience with isolation of Toxoplasma, there is every reason to believe that the organisms could be recovered from many eyes in which even the most arduous microscopic search of serial sections would fail to reveal them. The experience of Sir Stewart Duke-Elder and his associates[24] with the microscopic examination of 32 enucleated eyes, in which they found definite Toxoplasmalike structures only in one but were uncertain in 17 others, is a good example of the limitations of the morphologic approach. Simultaneous serologic studies on all patients as well as similar tests and studies on eyes that are enucleated for other reasons would provide suitable controls. It seems to me that there is a great need for the definitive information that such studies could provide. In contrast to this type of investigation in a few selected and properly staffed centers, I believe that little or

TABLE I

SUMMARY OF PRESENT KNOWLEDGE OF HUMAN TOXOPLASMOSIS

Human Toxoplasmosis

Congenital	Postnatal
1. *Fatal in utero*—chiefly central nervous system	1. *Typhuslike illness with or without pneumonitis—mostly fatal*
2. *Fatal first months of life* a. central nervous system and eyes b. Rash, jaundice, hepatosplenomegaly	2. *Encephalitis with or without rash* Duration—weeks; some fatal
3. *Survivors exhibit:* a. Severe damage to central nervous system and eyes (helpless "vegetables") b. Psychomotor retardation, and/or convulsions, chorioretinitis and cerebral calcification c. Chorioretinitis only or with focal cerebral calcification d. Hypothetically latent pseudocysts in eyes which in later years may be activated to produce chorioretinitis	3. *Benign lymphadenitis* a. Acute febrile—may last weeks b. Afebrile c. Subclinical d. Chorioretinitis—rare (1 in 100—Siim)
	4. *Inapparent or unrecognized* "Allergic" chorioretinitis—a rare complication

nothing would be gained from the routine use of Toxoplasma serologic and skin tests by individual ophthalmologists.

In conclusion, I should like to present in outline form a summary of our present knowledge of the clinical manifestations of human toxoplasmosis (table 1).

Elland Avenue and Bethesda (29).

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ATROPHY OF THE STROMA OF THE IRIS*

ENDOTHELIAL DYSTROPHY, CORNEAL EDEMA, AND GLAUCOMA

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Essential progressive atrophy of the iris is a disease long recognized and many times described in the literature. It is characterized by atrophy of the stroma of the iris which progresses to complete hole formation, single or multiple; the pupil becomes eccentric early. Ultimately glaucoma ensues from occlusion of the filtration meshwork by peripheral synechias or cuticular membranes. Many of the eyes have been lost from glaucoma but, in a few reported cases, the glaucoma has been arrested by successful surgical procedures.[1-3] Nothing is known as to the cause of the disease or as to the cause of the anterior synechias. Feingold[4] and, more recently, Heath[5] have advanced the theory that the iris atrophy is due to ischemia from vascular occlusion. Verhoeff in a discussion of Heath's paper suggested that the condition is analogous to essential atrophy of the choroid, so-called choroideremia. He thought it more likely that in both of these conditions the vascular changes were the result rather than the cause of the atrophy. Friedenwald in discussing the same paper was of the same opinion.

In only a few of the reported cases has any mention been made of the cornea until the disease was advanced and the tension quite high. Sugar[2] reported a case in which the vision was blurred in the morning and epithelial edema was noted when the tension was only 26 mm. Hg (Schiøtz). In this case there was marked iris atrophy with disappearance of approximately one half of the iris. There was a history of deformity of the pupil for seven years.

Zentmayer[6] briefly reported a similar case before the College of Physicians in Philadelphia. The patient was a man, aged 23 years. He had seen haloes about lights at times and complained of foggy vision in the morning. The cornea was "hazy." The iris presented in its nasal quadrant a partial atrophy of the stroma. Tension was 30 mm. Hg.

Ellett[7] gave a brief report on a 37-year-old patient with multiple holes in the iris. When first seen, the patient gave a history of blurred vision and seeing haloes around lights but tension was always normal. During the last year of observation, he noted at times "some disturbance of the corneal epithelium," and on two occasions blebs were observed in the lower cornea. The patient was observed over a period of four years.

Löhlein,[8] in 1951, reported a case of atrophy of the stroma of the iris in both eyes. In the right eye, only a small area of atrophy was observed (fig. 1). Tension was 22 mm. Hg. Gonioscopy showed the angle to be narrow but open. The pupil was round. In the left eye, the pupil was slightly oval. There was extensive atrophy of the stroma of the iris. Tension was 35 mm. Hg. Gonioscopy showed extensive peripheral anterior synechias.

In 1953, Pau[9] gave a further report on the same case. There was a history that, for six months, there had been periodic attacks of redness, tearing, and pain in the left eye. At first the attacks came every 10 days, then every four or five days. The cornea at various times showed large and small bullae, abrasions, and thickened cloudy stroma. There were fine pigment dots on the pos-

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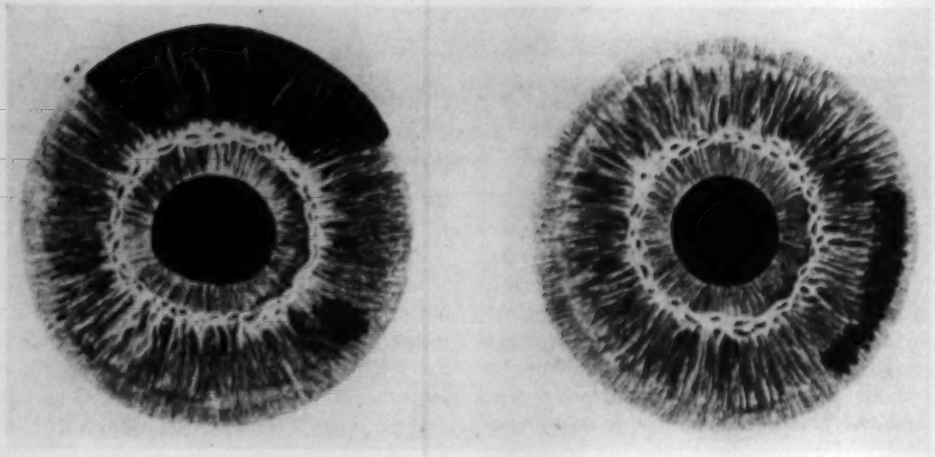

Fig. 1 (Chandler). From Löhlein. Extensive atrophy of the stroma of the iris in the right eye, slight in the left.

terior surface. The iris stroma was largely absent; only from the 10- to 12-o'clock and 2- to 3-o'clock positions was some of the iris stroma left but even this was rarefied and atrophic. The pigment layer and sphincter were intact. The pupil reacted normally. There were gross peripheral anterior synechias. Tension in spite of miotics was 50 mm. Hg (Schiøtz). Vision, depending on the condition of the cornea, ranged from 6/8 to 6/18. The field was full. In the right eye the appearance was the same as described by Löhlein. There was an area of slight stromal atrophy temporally. Tension ranged from 25 to 28 mm. Hg (Schiøtz). Vision equaled 6/5. A trephination was done on the left eye, which resulted in a tension of 15 to 20 mm. Hg (Schiøtz) but the attacks of pain continued and even came more frequently. The entire cornea was then covered with a conjunctival flap. New vessels grew into the cornea, the edema disappeared, and the eye remained quiet and comfortable.

The purpose of this communication is to present a syndrome which is probably a form of progessive essential atrophy of the iris but which presents somewhat different features than the usual case of essential atrophy.

The syndrome is characterized by slight atrophy of the stroma of the iris, peripheral anterior synechias, mild glaucoma, dystrophy of the posterior corneal surface and corneal edema. The points of difference from the typical case of essential atrophy are that in the cases to be reported, the atrophy of the iris is very slight and confined to the stroma with no hole formation, the pupil has remained central and round or only slightly oval, the glaucoma though not severe apparently appeared early in the disease, rather marked corneal dystrophy of the affected eye only is present in all cases, and in all but one case the presenting and most troublesome symptom has been edema of the cornea. Corneal edema causing blurred vision and colored haloes about lights has occurred with tension in the normal range or slightly elevated and before the eye was damaged by glaucoma.

Case reports

Case 1

S. S., a woman (MEEI773954), aged 47 years, was first seen in the clinic of the Massachusetts Eye and Ear Infirmary on April 2, 1952.

Examination. The right eye was externally and internally normal. In the left eye, the

pupil was slightly oval. There was rather marked dystrophy of the posterior corneal surface. There was an area of atrophy of the stroma of the iris near the periphery at the 1-o'clock position and another area near the limbus at the 7-o'clock position (fig. 2).

Gonioscopy of the right eye showed a normal open angle. In the left eye there was a broad anterior synechia up to Schwalbe's line from the 6:30- to 8:30-o'clock and from the 11:30- to 12:30-o'clock positions. Tension was: R.E., 21 mm. Hg; L.E., 27 mm. Hg (Schiøtz). Tonography showed outflow in the normal range in both eyes but definitely poorer in the left eye. There was a history of periodic blurred vision in the left eye.

In May, 1954, there was epithelial edema in the left eye. Tension was: R.E. 16 mm. Hg; L.E., 26 mm. Hg. Two-percent pilocarpine, four times a day, was prescribed for the left eye. During the next several months tension ranged from 21 to 24 mm. Hg. At most visits, slight epithelial edema was noted. On October 10, 1953, an iridectomy from the 9-o'clock to 11-o'clock positions was done. During the next six months tension in the left eye ranged from 19 to 26 mm Hg. Epithelial edema was noted at most visits. It was noted that the higher the tension recorded, the more prominent the corneal edema.

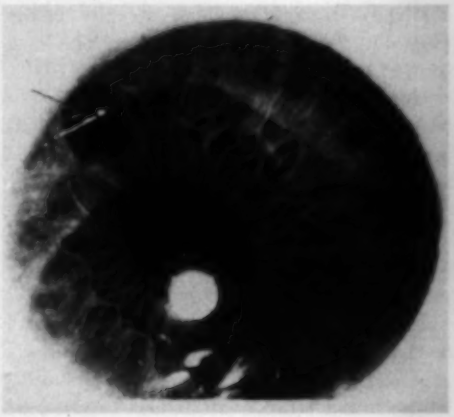

Fig. 2 (Chandler). *Case 1.* Arrow indicates area of atrophy of the stroma of the iris. Pupil is slightly eccentric.

Case 2

M. B., a man, aged 49 years, was first seen December 27, 1951, with a history of periodic blurred vision and seeing colored haloes around lights for several months. Glaucoma had been diagnosed by another oculist and a miotic prescribed. The symptoms continued but were less severe. Lately he has been using DFP every third day.

Examination. The left eye was externally and internally normal. There was no dystrophy of the cornea. Tension was 22 mm. Hg (Schiøtz). Gonioscopy showed a normal open angle. In the right eye there was a small patch of atrophy of the stroma of the iris between the 4- and 6-o'clock position (fig. 3). The pupil was slightly oval, two by three mm. There was a slightly wider rim of uveal pigment around the pupillary border in this eye than in the left eye. The cornea showed well-marked dystrophy of the posterior surface. This was characterized by a fine hammered silver appearance similar to Fuchs' dystrophy but less coarse than in the latter. The fundus was normal. The field was full. Tension was 28 mm. Hg. Gonioscopy

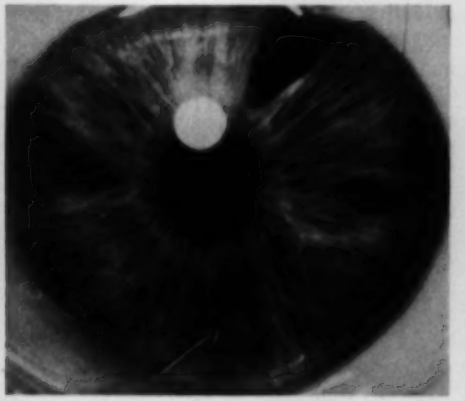

Fig. 3 (Chandler). *Case 2.* Arrow indicates area of atrophy of the stroma of the iris below. The pupil is pointed slightly downward. Peripheral iridectomy and portion of filtering scar at the 11-o'clock position.

showed scattered anterior synechias nearly or quite up to Schwalbe's line except nasally, where the angle seemed wide and open. Pilocarine (four percent every three hours) was prescribed. Two weeks later tension was: R.E., 25 mm. Hg; L.E., 19 mm. Hg. Several episodes of blurred vision and seeing haloes about lights had occurred since the last visit.

On January 28, 1952, tension was: R.E., 35 mm. Hg; L.E., 22 mm. Hg. He was given epinephrine bitartrate (one percent) to use twice a day in addition to the pilocarpine.

On February 1, 1952, tension was: R.E., 22 mm. Hg. Haloes had been seen only once since last visit. On February 26, 1952, tension was R.E., 32 mm. Hg. Several episodes of blurred vision and haloes since last visit. Slight to marked epithelial edema was noted on most examinations.

On March 29, 1952, a trephining operation was performed on the right eye. A good filtering scar developed. During the next nine months, tension in the right eye ranged from 13 to 17 mm. Hg. The patient remained completely symptom free.

On January 2, 1953, tension was: R.E., 25 mm. Hg. The filtering scar looked patent and unchanged. There had recently been one episode of seeing haloes about lights. Massage of the eye was advised.

During the next seven months tension ranged from 22 to 25 mm. Hg, usually 25 mm. Hg. There were occasional episodes of blurred vision and seeing haloes about lights. On January 26, 1954, massage was continued and four-percent pilocarpine, four times daily, was prescribed. During the next seven months tension ranged from 17 to 22 mm. Hg. There were very rare episodes of seeing haloes about lights. Vision with correction at the last visit equaled 6/5. The disc was normal.

Case 3

E. H., a woman, aged 41 years, was first seen by another oculist in February, 1951. There was a history of periodic blurred vision and seeing colored haloes about lights for several months. Tension was found to be 45 mm. Hg (Schiøtz). Pilocarpine (one percent, four times daily) was prescribed. The patient was first seen by me on April 5, 1951.

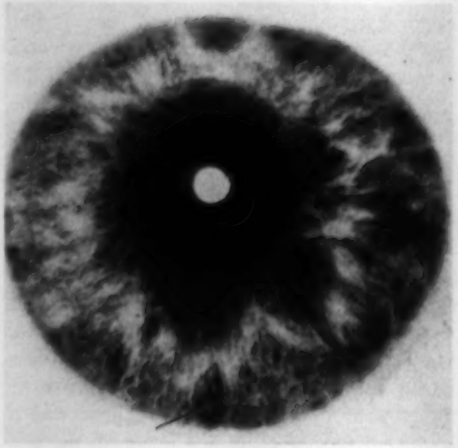

Fig. 4 (Chandler). *Case 3* Arrow indicates small area of atrophy of stroma of the iris.

Examination. The left eye was externally and internally normal. Tension was 15 mm. Hg (Schiøtz). In the right eye the cornea showed slight epithelial edema and a grayish finely stippled appearance of the endothelium, most marked in the central zone. The anterior chamber was of normal depth. The iris showed slight stromal atrophy below (fig. 4). The media were clear. The disc showed glaucomatous cupping.

Gonioscopy showed very extensive peripheral anterior synechias (fig. 5), consisting of thin strands of iris stroma attached to the trabecular wall, to Schwalbe's line, or onto the cornea itself. The synechias extended all the way around, except for essentially normal angle at the 9- and 2-o'clock positions.

In the left eye, the angle was wide and open and appeared normal, except for small areas at the 6- and 10-o'clock positions, where broad strands of light-colored tissue bridged the peripheral furrow from iris to trabecular wall, and where in the iris pe-

Fig. 5 (Chandler). *Case 3.* Gonioscopic picture of an area showing peripheral anterior synechias.

riphery there were little patches of stromal thinning.

Tonography showed a normal facility of outflow in the left eye, markedly reduced in the right eye. Tension in the right eye was 32 mm. Hg (Schiøtz). Corrected vision equaled 6/5 in both eyes. In the right eye there was a 25-degree upper nasal step and an enlarged blindspot. The field in the left eye was normal. Operation was advised.

On April 28, 1951, a trephining operation was done on the right eye. Since that time tension in the right eye has ranged from 22 to 16 mm. Hg. For the past three years, it has not been higher than 18 mm. Hg. Tension in the left eye has always been 15 or 16 mm. Hg. The patient has remained symptom free. There has been no further field loss. There has appeared to be little if any progression of the iris atrophy. The cornea still shows a grayish dystrophy of the posterior corneal surface. The cornea in the left eye appears completely normal.

CASE 4

L. C., a woman, aged 42 years, for the past few months, had had blurred vision in the left eye intermittently. It was usually worse in the morning, clearing during the day. Colored haloes had been seen at times. She consulted an ophthalmologist who found the tension to be 30 mm. Hg (Schiøtz), the cornea edematous, especially in the central zone. The condition was diagnosed as corneal dystrophy and the epithelium was removed from the central cornea. The epithelium failed to heal, bullae developed intermittently, and the patient experienced severe pain and lacrimation.

Examination. When first seen by me on September 2, 1952, the left eye showed profuse lacrimation. The cornea was edematous throughout, with stromal edema in the center, epithelial edema in the periphery. There were bullae in the lower central cornea and some areas of loss of epithelium. There was a small area of atrophy of the stroma of the iris two to three mm across opposite the 1-o'clock position (fig. 6). Tension to palpation was high normal. The right eye was externally and internally normal. Corrected vision was 6/5.

The patient was treated in the hospital with a binocular dressing and bland ointments. The epithelium healed and the patient became comfortable but epithelial edema persisted. In a few days bullous keratitis with severe pain recurred. The patient was readmitted to the hospital. The corneal epithelium was removed, the cornea curetted lightly and cauterized with 25-percent trichloracetic acid. A conjunctival flap was brought up from below, covering the lower three fifths of the cornea. The eye promptly quieted down and remained comfortable.

It was never possible to see the fundus

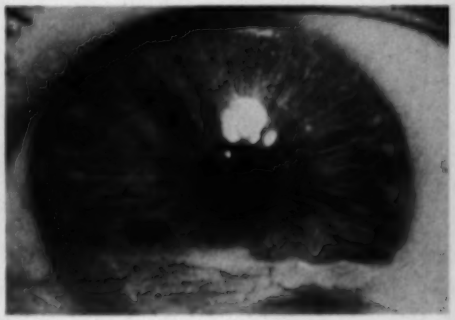

Fig. 6 (Chandler) *Case 4.* Arrow indicates area of atrophy of the stroma of the iris. Conjunctival flap can be seen covering lower portion of cornea.

but the visual field remained normal. Tension to palpation was estimated to be 30 to 35 mm. Hg. The flap retracted slightly above, exposing the pupil. A varying degree of epithelial edema was always noted. It was always worse in the morning, clearing somewhat later in the day.

Gonioscopy was first done in May, 1954. Due to the cloudiness of the cornea a clear picture could not be obtained. Anterior synechias could be seen here and there all around the angle. In places, especially opposite the area of stromal atrophy, the iris was attached to the cornea anterior to Schwalbe's line. It was estimated that approximately half the angle was free. Gonioscopy of the right eye revealed a normal open angle.

On May 19, 1954, the conjunctival flap was removed from the cornea of the left eye. Two weeks later the patient experienced some pain and one bulla was noted in the lower central cornea. This subsided and the patient remained comfortable. Epithelial edema persisted, always worse in the morning.

On September 3, 1954, tension by tonometer was 34 mm. Hg. The patient had been using two-percent pilocarpine, four times a day. On October 4, 1954, tension in the left eye was 40 mm. Hg. On October 22, 1954, a trephining operation was performed. A good filtering scar has developed and postoperatively tension has been 13 to 15 mm. Hg. There has been no corneal edema since the operation. The eye is quiet and comfortable.

CASE 5

K. S.,* a man, aged 36 years, was first seen in July, 1953, with a history of blurred vision in the right eye off and on for six months. In the left eye, vision was 6/5. Tension was 19 mm. Hg. Externally and internally, the eye seemed normal. Gonioscopy showed a normal open angle.

* This case is reported through the courtesy of Dr. Arthur C. Morrissey.

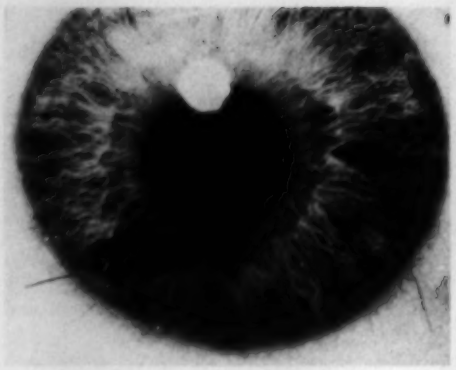

Fig. 7 (Chandler). *Case 5.* Arrow indicates area of atrophy of the stroma of the iris.

In the right eye, vision was 6/6−. There was considerable epithelial edema and rather marked dystrophy of the posterior corneal surface. The anterior chamber was normal. An area of atrophy of the stroma of the iris was seen down and temporally (fig. 7). The pupil was round and central and reacted normally. Tension was 19 mm. Hg.

Gonioscopy showed at the 4:30-o'clock position, a broad anterior synechia up beyond Schwalbe's line (fig. 8). From the 4:30- to 5:30-o'clock position, the iris was attached further forward than elsewhere but little if any beyond the scleral spur. From the 5:30- to 7:30-o'clock position, there was an anterior synechia up to Schwalbe's line. The remainder of the angle was wide and open.

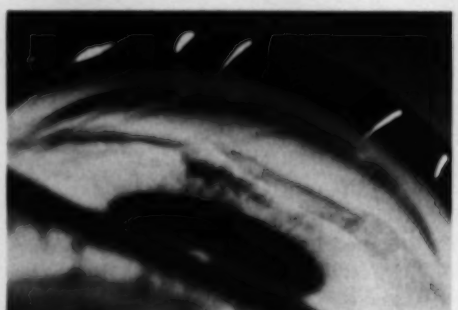

Fig. 8 (Chandler). *Case 5.* Gonioscopic picture, showing peripheral anterior synechias.

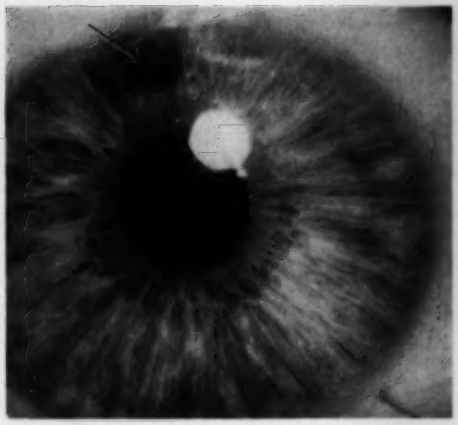

Fig. 9 (Chandler). *Case 6.* Arrow indicates small area of atrophy of the stroma of the iris. The pupil is pointed slightly upward.

One-percent pilocarpine, three times daily, was prescribed. During the next year and a half tension ranged from 20 to 23 mm. Hg. On most visits epithelial edema was present. On September 20, 1954, tension was 29 mm. Hg and corneal edema was marked. On October 8, 1954, tension was: R.E., 27 mm. Hg and there was marked epithelial edema. The gonioscopic picture was unchanged. Iris atrophy was unchanged. Vision with glasses was 20/40−. A trephining operation is scheduled for the near future.

Case 6

M. C.,* a woman, aged 35 years, was first seen on December 4, 1946, for refraction. Pupils were equal, round, and reacted normally. Vision was: O.U., 6/5, with correction. Both eyes were normal except for considerable dystrophy of the posterior corneal surface of the right eye only.

On December 8, 1950, examination was unchanged except that the right pupil was pear-shaped and pointed upward. On December 16, 1952, the right pupil was the same. The dystrophy of the right eye was the same. Gonioscopy showed one peripheral anterior synechia up to Schwalbe's line at the 12-o'clock position. Tension, O.U., was 14 mm. Hg. On April 6, 1953, the examination was unchanged. Tension was: O.U., 14 mm. Hg, as it was on September 10, 1953.

Fig. 10 (Chandler). *Case 6.* Gonioscopic picture, showing peripheral synechias.

On March 16, 1954, the examination showed no changes. Tension was: O.U., 16 mm. Hg. On September 14, 1954, tension was: R.E., 16 mm, Hg; L.E., 17 mm. Hg. The pupil and cornea were the same. There was an area of slight stromal atrophy above (fig. 9). Gonioscopy of the left eye revealed a normal open angle. In the right eye there was an anterior synechia up to Schwalbe's line from the 11- to 1-o'clock position (fig. 10). Below, some whitish tissue from the periphery of the iris obscured the ciliary band and seemed to be attached about at the level of the scleral spur. Corneal edema had not been noted at any examination.

Comment

Aside from Case 6, which as yet has not shown corneal edema or glaucoma, the common features in all the cases reported are dystrophy of the posterior corneal surface, corneal edema, atrophy of the stroma of the iris, and glaucoma. One or the other feature may predominate in a given case. In Cases 1, 2, 4, and 5 corneal edema was the most prominent symptom. In Case 4 it was a serious problem. Only in Case 3 had the eye been damaged by glaucoma. In Case 3 there was only one small area where the iris stroma

* This case is reported through the courtesy of Dr. Carl C. Johnson.

was entirely absent, though the whole iris transilluminated much more readily than in the fellow eye. The pupil was slightly distorted in Cases 1 and 2 but was central. In Case 6 the pupil was displaced slightly upward. The pupil was round in Cases 3, 4, and 5. In all cases any small increase in intraocular pressure caused edema of the cornea.

In all of the cases, dystrophy of the endothelium of the affected eye only was noted in slitlamp examination. In all cases the endothelium must be assumed to be functionally defective, since with a normal endothelium a much higher tension is required to produce corneal edema. In Case 6 tension has never been higher than 16 mm. Hg and corneal edema has not been noted. In Case 5 the cornea showed epithelial edema with a tension of 22 mm. Hg. In Case 3, when the tension reached 25 mm. Hg, epithelial edema was manifest. Thus far it appears that if tension can be maintained below 20 mm. Hg, the cornea remains clear. Aside from Case 3 the glaucoma has not been a real problem as regards loss of function.

Increased tension is a real problem, however, from the standpoint of the cornea. From experience thus far with Cases 2, 3, and 4 a successful trephining operation has had a very favorable effect on the cornea. In Case 2, massage and miotic therapy are necessary to keep the tension low enough to keep the cornea clear. Considerably more time must elapse before one can be sure of the permanence of the operative results. With the passage of time, the iris atrophy may well progress to eccentricity of the pupil and complete holes in the iris, as in the ordinary case of essential iris atrophy.

Case 6 represents the earliest manifestation of the syndrome. Though dystrophy was noted in 1946, slight eccentricity of the pupil was not noted until four years later. In this case, tension has remained 16 mm. Hg or less and no corneal edema has developed thus far.

Pau's case was very similar to the cases reported, except that the iris atrophy was more advanced and the glaucoma more severe than in any of the cases here reported.

In the light of experience gained in the observation of the cases herein reported, it would appear that the problem of corneal edema was of equal, if not greater, importance than that of increased tension. In Pau's case the corneal changes were apparently irreversible, since even with a low tension after trephination, bullous keratitis persisted. The ineffectiveness of iridectomy in preventing corneal edema is illustrated in Case 1.

It is realized that the number of cases observed is too small and the period of observation too short to draw valid conclusions. However, it would appear that a filtering operation should be done early, not only because of the glaucoma but especially because of the cornea.

Summary

1. Six cases are reported of a syndrome of atrophy of the stroma of the iris, corneal dystrophy with edema, peripheral anterior synechias, and glaucoma. There were two men and four women with ages ranging from 36 to 49 years. The disease is unilateral in all cases.

2. A prominent feature and a presenting symptom in all but one early case was edema of the cornea, which occurred with normal or only slightly increased intraocular pressure. All cases showed unilateral dystrophy of the posterior corneal surface.

3. An early filtering operation would appear to be indicated, both from the standpoint of the corneal edema and the glaucoma.

5 Bay State Road (15).

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HEREDITARY CONGENITAL OPHTHALMOPLEGIA*

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Chronic external ophthalmoplegia has been brought to the attention of the American Ophthalmologic Society on two previous occasions. Friedenwald,[1] in 1922, and Langdon and Cadwallader,[2] in 1928, presented case histories of patients with this affliction. Their accounts were similar to von Graefe's original description in 1856 and Hutchinson's[3] detailed studies in 1878. Bilateral ptosis and practically complete loss of motion of both eyes, associated with normal pupillary responses, were the principal findings in their patients. The onset of the disease occurred from infancy to over 50 years of age. The incidence in males and females was about equal. None of these patients showed physical or neurologic signs indicating systemic disease elsewhere in the body.

The family that came to my attention has 19 members. Of these nine had the disease since birth. None of them exhibited other congenital physical defects or mental disturbances. The inheritance in this family was a congenital, nonprogressive, nonsex-linked, dominant characteristic. It was similar to the 16 cases in five generations descriped by Bradburn[4] and the five cases in two generations reported by Faulkner.[5] The disease combined with miosis has, however, been transmitted as a recessive trait in a family described by Gates.[6]

CASE REPORT

I was fortunate in getting moving pictures of eight of the affected members who represented three generations. Of these, I was able to examine and study only one in detail.

History. This patient was a 27-year-old, single,Chinese male. He had bilateral ptosis with almost complete external ophthalmoplegia and rotatory nystagmus. His ptosis and ophthalmoplegia were not influenced by administration of Prostigmin or alphatocopheral. Neither were they affected by emo-

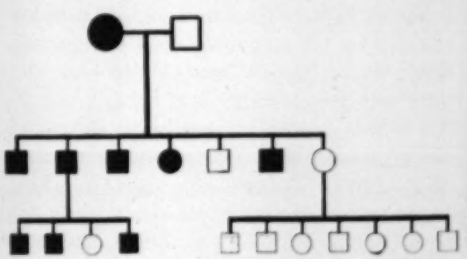

Fig. 1 (Holmes). Pedigree, illustrating hereditary transmission of external ophthalmoplegia in three generations.

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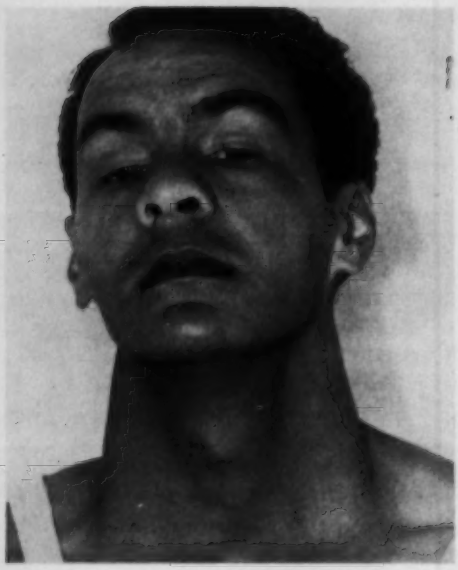

Fig. 2 (Holmes). Bilateral ptosis and hypertrophy of both sternocleidomastoid muscles.

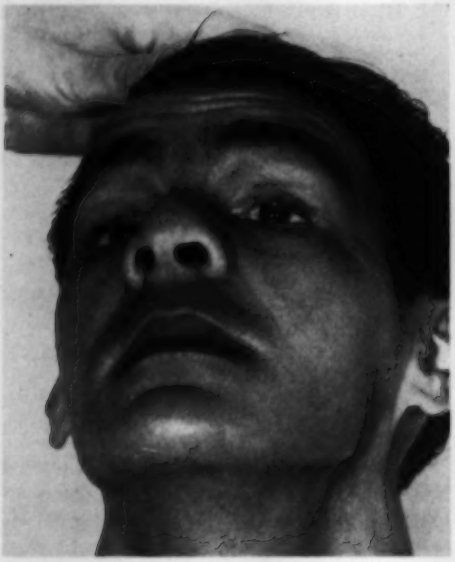

Fig. 3 (Holmes). Hutchinsonian facies, demonstrating wrinkles in forehead, extension of neck on attempted forward gaze.

tional disturbances, straining, or fatigue.

In an effort to see beneath his drooping eyelids, he had to wrinkle his forehead and throw his head backward, assuming the Hutchinsonian facies. He was totally unable to move his eyes in the vertical and oblique directions. In the horizontal meridian and on attempted convergence, his eye movements were limited to "minimal excursions" amounting to zero to five degrees on adduction and to two to three degrees on abduction. He had never been troubled with diplopia.

Vision in his right eye was 5/400; in his left, 20/40. His accommodation was normal. With his left eye he was able to read and carry out his duties as a plumber's helper. His pupils reacted promptly to light and convergence. His ocular media and fundi were normal. Refraction revealed a slight myopic error. However, his vision could not be improved with lenses. The intraocular pressure of both eyes was within normal limits.

Slitlamp examination was noncontributory. Peripheral visual field studies, plotted with three-mm. white and colored test objects, failed to reveal defects or scotoma.

Physical examination was normal save for

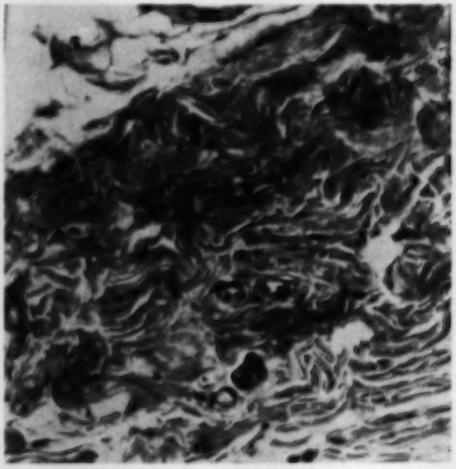

Fig. 4 (Holmes). Complete replacement of the external rectus muscle by hyalinized, relatively cellular fibrous tissue.

the fact that he had a powerful muscular physique with specially overdeveloped sternocleidomastoid muscles. This was probably partly due to his hobby as a physical culture faddist rather than to prolonged, faulty position of his head on attempted upward gaze. Neurologic examination by Dr. R. B. Cloward was negative.

Laboratory examinations, including blood count, blood chemistry, urinalysis, blood and spinal serology, basal metabolism rate, skull and sinus X-ray studies, and encephalographic tracings were within normal limits. A biopsy taken from the belly of the right external rectus revealed:

"Complete replacement of muscle tissue by hyalinized relatively acellular fibrous tissue. Special stain verifies that this is collagen. There are no evidences of a dystrophic process such as increased fat, variation in size of muscle fibers, and giant muscle fibers." Chemical analysis of the biopsied muscle was not done.

Discussion

In the absence of pathologic reports of the nuclear areas from cases of bilateral, congenital, external ophthalmoplegia, various theories have been advanced to explain these anomalies. Embryonic, supranuclear, nuclear, nervous, and muscular aberrations have been implicated.

An abnormal embryonic development at the encephalic flexures has been suggested by Helfand.[7] A congenital deficiency in the anlage of the ocular muscles was assumed to be responsible by Uthoff.

A supranuclear origin of the disease was proposed by Wilson who was able to elicit free movements of the eyes upon stimulation of the optic fixation reflexes.

The nuclei of the oculomotor nerves have been believed to be responsible by Moebius[8] who thought there was an actual absence of the nuclei; by McMullen and Hine[9] who attributed the affection to defective nuclear development; and by Langdon and Cadwallader[2] who, on the basis of autopsy findings, ascribed the disease to degeneration of the nuclei of the third, fourth, and sixth nerves, with sparing of the Edinger-Westphal nuclei. Ida Mann[10] showed that the Edinger-Westphal nuclei which regulate the pupillary responses receive their innervation from the subcortical and cortical regions independently of the oculomotor nerve roots.

A purely muscular, rather than a nuclear or nervous background, was proposed by Gourfein.[11] On the basis of muscle biopsy from the lids of five patients with congenital ptosis, Fuchs[12] likewise believed that the disease represented a myopathy of the extraocular muscles. Li[13] at surgery found defective rectus muscles in two patients with this disease. He assumed that this was congenitally present and was not the aftermath of continued disuse. Ida Mann[10] believed that the condition might be muscular abiotrophy since the intrinsic muscles, two of which are ectodermal, and so not comparable with the recti, always escape. Kiloh and Nevins[14] and Adams, Denny-Brown, and Pearson felt that these cases represent a special form of muscular dystrophy. Brown[15] reported three patients with bilateral ptosis associated with paralysis of the extraocular muscles. At surgery, he found the four recti to be fibrous bands. He termed the disease "fibrosis syndrome."

Lewandowski, on anatomic grounds, doubted that the disease could exist as an independent entity. He believed it was associated with other neurologic diseases, such as tabes, amyotrophic lateral sclerosis, Wernicke's hemorrhagic superior polioencephalitis, and myasthenia gravis. His objections, however, are not valid, as the disease is known to exist as an isolated syndrome.

I am inclined to agree with deSchweinitz[16] that the condition may be best explained by assuming the combined influences of nuclear aplasia or dysplasia associated with imperfect development and structural defects of some or all of the external ocular muscles.

The prognosis for life is good. Treatment

is of no avail. Crutch glasses have been recommended for the ptosis.

It is hoped that continued researches may clarify our understanding of this uncommon, deforming disease. Studies of hereditary patterns may reveal faulty linkages of the involved genes. Biochemical assays of the urine and blood for creatine and creatinine and of the involved muscles for their creatine, acid-soluble phosphorus, phosphocreatinine, and adenosine triphosphate content may reveal a lack of these substances. Electromyographic tracings of the individual eye muscles may furnish further clues in differentiating between a neurogenic and myogenic background for this disease.

Lastly, pathologic examination of brains from patients with this disease remains the most important but still relatively unexplored avenue for future investigation.

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Ophthalmic Miniature

A lady's portrait has been known to come out of the finishing-artist's room ten years younger than when it left the camera. But try to mend a stereograph and you will soon find the difference. Your marks and patches float above the picture and never identify themselves with it. . . . No woman may be declared youthful on the strength of a single photograph; but if the stereoscopic twins say she is young, let her be so acknowledged.

Oliver Wendell Holmes: Sun-painting and sun-sculpture, *Atlantic Monthly*, 1897.

EXPERIMENTAL APPROACH TO THE PATHOGENESIS OF RETROLENTAL FIBROPLASIA*

IV. The effects of gradual and of rapid transfer from concentrated oxygen to normal air on the oxygen-induced changes in the eyes of young mice

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Introduction

It is generally agreed that a higher incidence of retrolental fibroplasia occurs if the premature infants have been exposed to high oxygen concentrations.[1-13] It has, however, not been definitely proved that oxygen is the immediate cause of the disease, and the possibility remains that other factors may contribute to its development. Oxygen has been shown in vivo to have a constrictive and possibly obliterative effect on the vessels of the retina both in infants[14] and animals.[15]

The disagreement concerns the point as to whether the early pathologic picture of proliferation of retinal vessels occurring in retrolental fibroplasia is caused by persistent hyperoxia or whether consecutive hypoxia is the precipitating factor, either local through retinal ischemia, or general due to, for example, anemia, hyaline membranes,[16] and pulmonary infections,[17] or rapid withdrawal from the high oxygen concentration ("a relative anoxia").[7,18]

The hyperoxygenation theory is supported by clinical observations[6,9,11,12] and animal experiments.[19] The opposite theory has been stressed by Szewczyk[21-23] and Bedrossian and co-workers,[7,18] and is also supported by animal experiments.[24-27]

Patz,[28] summarizing the experiences from clinical and experimental studies made by him and his co-workers, states that withdrawal from oxygen is not essential for oxygen to be injurious, but that the data suggest that if the infant (or animal) is rapidly removed from a high oxygen environment during a stage of marked retinal vasoconstriction an additional injury is induced by a state of retinal anoxia. Finally, a gradual reduction of the oxygen concentration in the incubator is recommended in the exceptional cases in which clinical indications have necessitated high concentrations of oxygen for a prolonged period.

Locke[9] seems to have had the same experience and his studies support the concept that prolonged high oxygen concentrations are injurious as a result of a direct effect. From his investigations cannot be deduced, however, whether rapid removal from high oxygen may increase the danger for retrolental fibroplasia, as all his cases were slowly weaned.

Szewczyk, in his latest report[23] based upon a broad clinical experience, argues that the disease can be induced in babies acclimatized to high amounts of oxygen by rapid reduction of available oxygen and that these changes can be prevented by gradual weaning to a normal atmosphere. Furthermore he states that the early stages of the disease regress following oxygen therapy.

The only controlled studies in this respect so far published have been made by Bedrossian and co-workers.[7,18] In the first report[7] premature infants were alternately placed in a group to be weaned from oxygen and a group to be suddenly withdrawn. Thirteen of 25 infants suddenly removed from oxygen developed retinopathy, whereas only two out of 24 who were weaned during 10 days developed the disease. The difference was statistically significant and furthermore the disease was much more severe in the group sud-

* From the Histological Department of Karolinska Institutet (Head: Prof. G. Häggqvist, M.D.) and the Pediatric Clinic, Karolinska Institutet (Head: Prof. A. Wallgren, M.D.). These studies were aided by grants from the Swedish National Medical Research Council.

dently withdrawn. The only objection to this investigation seems to be the difference in the initial oxygen concentration between the two groups, this being 60 percent for the infants rapidly withdrawn and 50 percent for those weaned. It cannot be excluded, from the data presented, that this difference might play a role concerning the observed different frequencies of the disease.

In a more recent controlled study[18] Bedrossian and co-workers report a significantly higher incidence of the disease in infants removed from an atmosphere of 50-percent oxygen than in a group where oxygen was gradually reduced from the same initial concentration. In this material five of 26 developed the disease when the oxygen was reduced to 40 percent and to 30 percent for four days. Three of 10 developed retrolental fibroplasia weaned in 35-percent oxygen for eight days. Of 16 infants treated with 50-percent oxygen for seven days and rapidly withdrawn, nine developed the disease, and six of nine also developed retrolental fibroplasia when the oxygen treatment was extended to 15 days, followed by rapid withdrawal. It is also stated that oxygen had a definitely beneficial effect on infants with progressive retinopathy.

The animal experiments by Ashton and co-workers[15, 24, 25] have shown conclusively that an abnormal proliferation of retinal vessels occurs when the animals are withdrawn from high oxygen concentrations. In our own studies[26] these changes have occurred to a high incidence when newborn mice were transferred to air, following five days' exposure to 100-percent oxygen. These results suggested a study to reveal whether the oxygen-induced changes of the eyes could be modified or prevented by weaning. No such study in animals has so far been presented.

Material and Methods

The same inbred strain of black mice was used as in our previous work (stock C 57 BL/6, Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine). The breeding of the mice, the standard food, the method for the exposures to oxygen mixtures, and the histologic technique were the same as previously described.[26, 27, 29] The flow and the concentration of the oxygen mixture were checked twice a day. The relative humidity was 80 to 90 percent and the temperature about 24° C.

The exposure to oxygen began within 16 hours after birth. The mothers of the young exposed to oxygen were interchanged, with mothers of litters of the same age, not exposed to oxygen, because the adult animals did not stand the high concentrations of oxygen more than a few days. This was done every second day. One half of a litter was as a rule grouped together with one half of another litter, born on the same day, making up the group to be weaned, and the two second halves were used as control animals rapidly withdrawn.

The following groups of animals, subjected to rapid or gradual diminishing of oxygen concentration were used:

Group 1 (53 animals survived)

The animals in this group were given 98- to 100-percent oxygen for five days, followed by a stay in air for (a) 10 or (b) 18 days (29 and 24 animals respectively), making these control animals similar in age when killed to the animals of Groups 2 and 3.

Group 2 (34 animals survived)

These animals received 98- to 100-percent oxygen for five days, 80 ± 3 percent for two days, 60 ± 3 percent for three days, 40 ± 3 percent for three days, followed by a stay in air for (a) two days or (b) 10 days (19 and 15 animals respectively).

Group 3 (10 animals survived)

In this group, 98- to 100-percent oxygen was given for five days, 60 ± 3 percent for two days, 40 ± 3 percent for three days, $30 \pm$

3 percent for three days, followed by a stay in the air for (a) two days or (b) 10 days (six and four animals respectively).

GROUP 4 (eight animals survived)

Exposure to 98- to 100-percent oxygen for five days followed by 60 ± 3 percent oxygen for 10 days.

GROUP 5 (seven animals survived)

These animals were given 98- to 100-percent oxygen for five days, 60 ± 3 percent oxygen for two days, and 40 ± 3 percent for 10 days.

GROUP 6 (13 animals survived)

Exposure to 98- to 100-percent oxygen for five days, 60 ± 3 percent oxygen for three days, 40 ± 3 percent for three days, and 30 ± 3 percent for 10 days.

Each change of oxygen concentration took place during a couple of hours, with the exception of the transfer to air, which was done abruptly without any gradual lowering of the oxygen concentration. The survival rate of the groups amounted to about half of the animals. Because of the small size of the groups and the different ages of the animals in various groups, no significant differences can be calculated as regards survival rate.

RESULTS

CHANGES OF THE VESSELS IN THE NERVE-FIBER LAYER

The most characteristic change of the eyes in the early stages of human retrolental fibroplasia is the irregular hyperplasia of the vessels in the nerve-fiber layer with hemorrhages and budding of capillary tufts into the vitreous body. Similar changes have been found in newborn and young mice, subjected to exposure to concentrated oxygen for five days, and subsequent rapid transfer to normal air (fig. 1). This has already been published previously[26, 27] and these findings were confirmed in the animals of Group 1 in the present investigation.

Hyperplasia of the vessels in the nerve-fiber layer, frequently with capillary tufts protruding into the vitreous body, were found in 26 of 29 animals after 10 days in air and in 13 of 24 animals after 18 days in air.

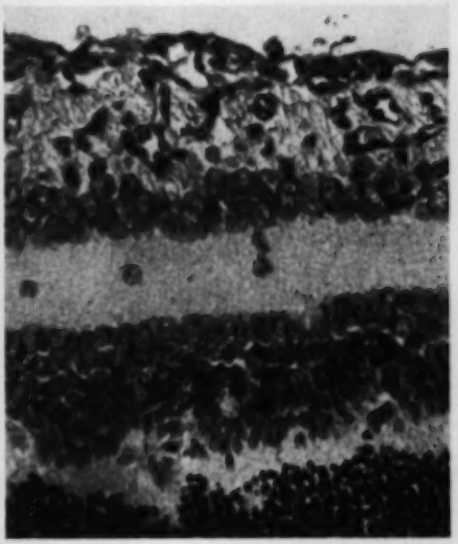

Fig. 1 (Gyllensten and Hellström). Exposure of newborn mouse to concentrated oxygen for five days, followed by stay in air for 10 days. Vascular proliferations in the nerve-fiber layer. (×400.)

In the animals of Groups 2 and 3, subjected to exposure to concentrated oxygen and gradual transfer to air, similar changes were found in nine of 19 animals after 10 days' stay in air. Animals belonging to Groups 2 and 3 and killed after only two days in air showed these vascular changes in only five of 25, probably illustrating the necessity of a stay in air, or at least lower concentrations, for some days before the typical hyperplasia develops.

Hemorrhages in the nerve-fiber layer were found in only one animal of 44 subjected to gradual transfer to air, in contrast to eight animals of 53 subjected to rapid transfer to air.

In all groups, the changes of the vessels in the nerve-fiber layer were mostly located in the neighborhood of the optic disc (fig. 2).

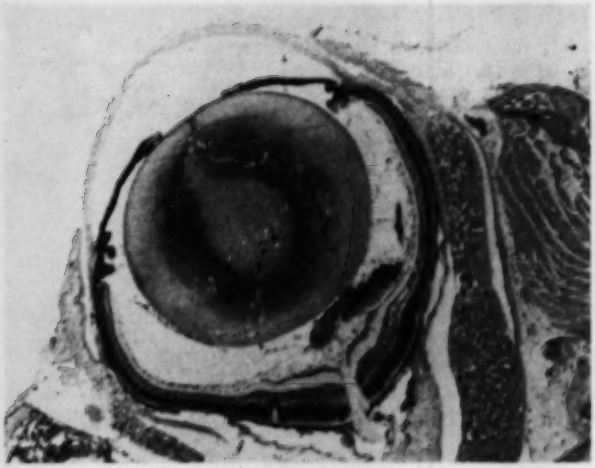

Fig. 2 (Gyllensten and Hellström). Exposure of newborn mouse to concentrated oxygen for five days, followed by stay in air for 10 days. Vitreous hemorrhage, thickening of the retina with proliferation of vessels in the nerve-fiber layer. The changes are mainly located in the neighborhood of the disc. (×30.)

In the animals gradually transferred to air, there was also initially a retarded outgrowth of vessels in the rest of the nerve-fiber layer, as contrasted with the animals rapidly transferred to air (figs. 3 and 4).

No significant difference was found between the animals of Groups 2 and 3 concerning these vascular changes.

From the above-mentioned figures it seems clear that the animals gradually transferred to air showed a retardment of retinal vascularization and also of the abnormal changes of the vessels in the nerve-fiber layer. After a longer stay in air, however, this difference between weaned and rapidly withdrawn animals diminished and no significant lessening

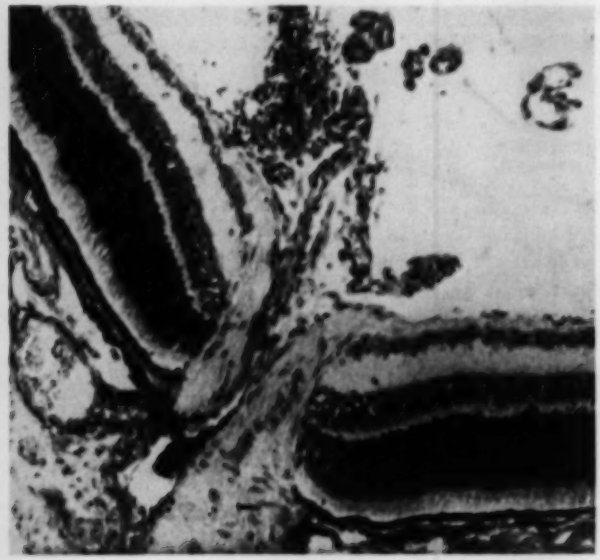

Fig. 3 (Gyllensten and Hellström). Exposure of newborn mouse to concentrated oxygen for five days, followed by gradual lowering of oxygen (Group 2) and subsequent stay in air for two days. Persistence of hyaloid vessels with small hemorrhages in the vitreous body. Absence of vessels in the nerve-fiber layer. (×200.)

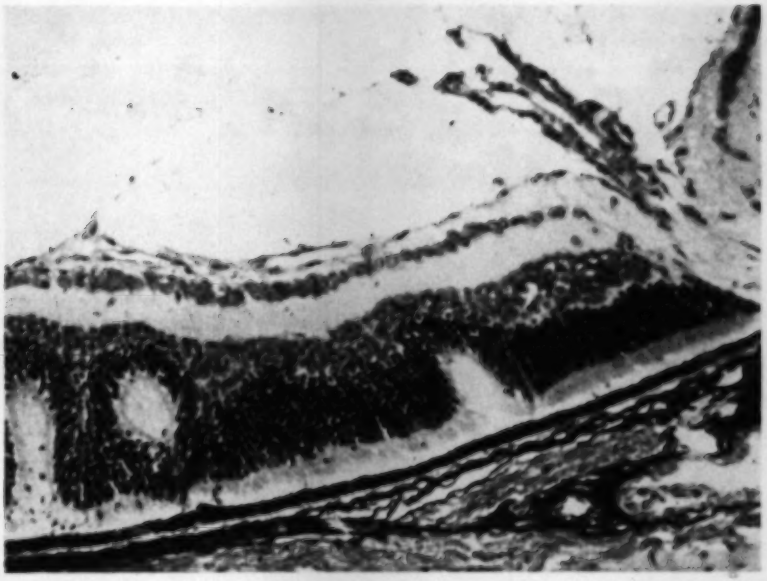

Fig. 4 (Gyllensten and Hellström). Exposure of newborn mouse to concentrated oxygen, followed by gradual lowering of oxygen (Group 3) and subsequent stay in air for 10 days. Persisting hyaloid vessels, outgrowth of vessels in the nerve-fiber layer. Sharp folds and partial fusion of nuclear layers. (×200.)

of the pathologic changes similar to those found in retrolental fibroplasia was seen after this more prolonged observation.

In the animals of Groups 4 to 6, which were exposed to concentrated oxygen and transferred to lower concentrations of oxygen but not to air, there was a retardation of the outgrowth of vessels in the nerve-fiber layer. No pathologic hyperplasia of retinal vessels occurred in Group 4. In Groups 5 and 6 such hyperplasia was frequently found (fig. 5). No hemorrhages were seen in the nerve-fiber layer.

Changes of the hyaloid vessels

The eyes of newborn mice are more immature as regards development, compared with the eyes of human newborn or viable premature babies. Functioning hyaloid vessels still persist. These vessels grow hypertrophic and hyperplastic in newborn mice, exposed to concentrated oxygen.[26, 27] In the animals of Groups 2 and 3, gradually transferred to air, there was a more conspicuous hyperplasia of these vessels than in animals of Group 1, rapidly transferred to air (fig. 3). After 10 days' stay in air, however, the hyperplasia of the hyaloid vessels had di-

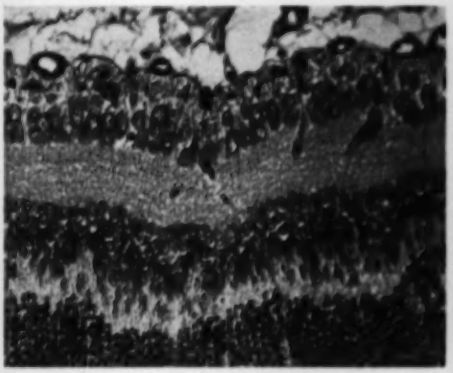

Fig. 5 (Gyllensten and Hellström). Exposure of newborn mouse to concentrated oxygen for five days, followed by gradual lowering to 40 percent (Group 5). The capillaries in the nerve-fiber layer are budding into the vitreous body. (×400.)

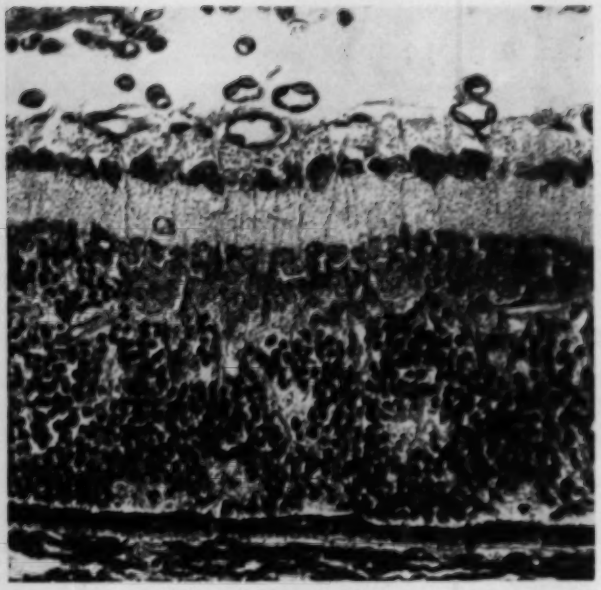

Fig. 6 (Gyllensten and Hellström). Exposure of newborn mouse to concentrated oxygen for five days, followed by gradual lowering of oxygen (Group 2) and subsequent stay in air for 10 days. Vessels in the nerve-fiber layer budding into the vitreous body, anastomosing with persistent hyaloid branches. Fusing and intermixture of nuclear layers. (×400.)

minished and was not more intense in the animals gradually transferred.

A characteristic finding was the occurrence of hyaloid vessels growing out from the stem in the neighborhood of the optic disc and creeping closely adjacent to the internal limiting membrane of the retina with anastomoses of the vessels in the nerve-fiber layer. This was found most regularly in animals gradually transferred to air.

Hemorrhages from hyaloid vessels, mostly in the vitreous body, were a frequent finding in all groups. No apparent difference between the Groups 1 to 3 was found as regards these hemorrhages. They occurred in 50 to 100 percent of the animals.

Fig. 7 (Gyllensten and Hellström). Exposure of newborn mouse to concentrated oxygen, followed by stay in air for 18 days. In the left half of the microphotograph atrophic changes mainly in the inner nuclear layer. No proliferation of retinal vessels is seen in this part of the retina. (×200.)

The animals of Groups 4 to 6 first exposed to concentrated oxygen and then to lower concentrations of oxygen but not to air, also exhibited similar hyperplasia of the hyaloid vessels, most in Group 4, least in Group 6, and hemorrhages from these vessels frequently occurred.

Changes of the retina with the exception of vascular changes

Irregularities of the retinal layers, especially fusing and intermixture of the nuclear layers (fig. 6) with the occurrence of small, sharp folds, and atrophic changes of the retina, mostly of the outer plexiform and inner nuclear layers (fig. 7), were frequently found in all groups. The atrophies showed a tendency to increase with advancing age of the animals. No connection was apparent between the method for the transfer to air and the frequency of these retinal changes. The atrophies were mostly located in the anterior parts of the retina. The irregularities were found mostly in the neighborhood of the optic disc, this location being especially predominant after rapid transfer to air.

The animals of Groups 4 to 6 also exhibited irregularities and atrophies of the retina, more so in Groups 5 and 6 than in Group 4. Compared with those animals of our previous experiments[26] which were exposed to concentrated oxygen for 16 days or less, the present ones, exposed to concentrated oxygen and gradual lowering to 60, 40, and 30 percent oxygen, showed a higher frequency of retinal abnormalities.

Discussion

The pathologic changes of the mouse eye, induced by exposure to oxygen of 98- to 100-percent concentration and subsequent transfer to air, show similarities with early stages of human retrolental fibroplasia. The similarities concern the abnormal vascularization of the nerve-fiber layer. There are, however, also many differences. The final, cicatricial stages of retrolental fibroplasia have never been reproduced experimentally. We have observed a number of mice for half a year after the transfer from concentrated oxygen to air. In all of these animals the vascular hyperplasia in the nerve-fiber layer and the hemorrhages disappeared. The only residue of the very conspicuous pathologic changes of the eyes has been slight atrophic changes in parts of the retina mostly situated anteriorly. The changes of the hyaloid vessels and the retinal irregularities and atrophies, found among the oxygen-induced abnormalities of the mouse eye, afford no apparent basis for the understanding of the pathogenesis of human retrolental fibroplasia.

The present investigation has demonstrated that the oxygen-induced disease of the mouse eye cannot be prevented by the gradual transfer to air, as performed in our experiments. The difference found between animals gradually transferred to air and those rapidly transferred are mainly only differences regarding the time schedule of the changes. Retarded outgrowth of the vessels in the nerve-fiber layer and consequent delay of the pathologic hyperplasia of these vessels were observed after gradual transfer to air compared with the animals rapidly transferred. As found by us previously,[27] however, older animals have a lesser tendency to oxygen-induced hyperplasia of the vessels in the nerve-fiber layer. The fact that the animals gradually transferred to air were older when they came into air than the animals rapidly transferred, may consequently also be responsible for the initial decrease in the vascular changes of the nerve-fiber layer in the former groups. This circumstance cannot be the decisive factor, however, as both normal and pathologic vascularization do occur when the animals are allowed to stay longer than two days in air. In a more prolonged process of weaning than used in our experiments, this age factor may possibly influence the picture to a higher degree and such an experiment might result in prevention of the eye changes. Such an experiment would, however, not be conclusive concern-

ing the possibilities of preventing the disease in infants in this way, as the postnatal maturation of the eyes of young mice is much more rapid than in premature children.

The animals of Groups 4 to 6 which were exposed to concentrated oxygen and subsequent transfer to lower concentrations of oxygen, but not air, show that the proliferations of retinal vessels may occur even in a higher concentration of oxygen than in air, the hyperplasia of vessels in the nerve-fiber layer occurring in concentrations below 60 percent. Compared with our previous work[28] when exposing newborn mice to concentrated oxygen for more than two weeks but not to any lowering of the oxygen concentration, the results in the present Groups 4 to 6 show that the lowering of the concentration gives a higher incidence of both vascular changes and irregularities of the retinal layer.

The other changes of the retina and of the hyaloid vessels, induced by oxygen in mice, were not influenced significantly as regards frequency by the method for the transfer to air.

Summary and Conclusions

1. The effect of gradual lowering of the oxygen concentration on the oxygen-induced disease of the eyes of young mice has been studied and compared with frequency and intensity of the eye changes in animals rapidly withdrawn.

2. The gradual lowering of oxygen concentrations resulted in an initial retardation of both normal and pathologic vascularization of the retina. Following a prolonged observation, however, with a longer stay in air, this difference was no longer obvious.

3. Changes of hyaloid vessels, irregularities, and atrophies of retinal layers are not significantly influenced by the method of transfer to air.

4. The study does not support the view that oxygen-induced changes of the eyes of mice can be prevented by a process of weaning.

5. It is pointed out that, although many similarities exist between the oxygen-induced changes of the mouse eye and the early pathology of retrolental fibroplasia, there are also many differences, especially concerning the final outcome of the respective diseases. Conclusions from animal experiments, including the influence of the process of weaning, should be drawn cautiously.

Solnavägen 1 (60).

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STUDIES ON RADIATION CATARACT*

I. Determination of the Threshold Dose Level of Radiation Cataract

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Although Rohrschneider[1] reported that the threshold level of the radiation cataract was equal to the epilation dose at a single exposure of X rays whose factors were 180 kv., with filters 0.5 mm. Cu and 3.0 mm. Al, that is, 890 r, and with only 3.0 mm. Al, 980 r; Peter,[2] employing 150 kv., reported 550 r. On the other hand, when fractioning irradiation was used, the epilation dose level was twice as high as the cataractogenic one, which remained at almost the same level with a single radiation. It was concluded that the lens has a much higher accumulating property than that of hair.

Aulamo[3] reported that the critical dose level was different from the quantity of X rays employed, that is, with soft rays, the dose was two epilation doses, and with hard rays three epilations. Employing 150 kv., with 0.5 mm. Cu and 1 mm. Al. K itajima[4] came to the conclusion that lens changes occurred at 69 percent unit skin dose, 216 r

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by histology and 103 percent unit skin dose, 324 r clinically.

Cogan,[6] who has conducted broad experiments on this problem with X rays and neutrons, concluded that lens changes resulting from irradiation did not have a critical dose and the lower the dose the less apparent were the changes, with the endpoint depending chiefly on the method of examination.

The term cataract is arbitrarily defined as a lens opacity that would result in some impairment of vision if it were to be present in human lens. This occurs in the rabbit lens with an irradiation of the following types and amounts: X rays, 500 r; neutrons, 8.4×10^9 particles cm.^{2} (examined only clinically during 18 months). With decreasing dosage the effect of irradiation of the lens decreases less rapidly with neutrons than with X rays.. To study the minimal dose tolerated by a human eye exposed to a known amount of X rays, the various steps were carried out following the clinical data by Rohrschneider,[1] Desjardins,[8] Poppe,[9] Leinfelder and Kerr,[10] Hunt,[11] Schulz and Heath,[12] and Cogan and Dreiser.[7]

The results in these experiments varied with respect to the cataractogenic level of the X-ray cataract. To decide it on the basis of clinical symptoms only is impossible because the incubation period may extend over several years during which time a senile opacity, such as thickening of the suture of the posterior pole region may develop; such a lesion is very much similar to the radiation cataract which, however, can be excluded by its histologic differences.

Materials and Methods[13]

White rabbits, aged three to four months, were exposed to X rays of the following factors: 80 kv., added filtration of 2.0 mm. Al, 12 cm. target skin distance; in doses ranging from 600 r to 2,000 r in single exposure and 150 r to 350 r two times a week, total 10 times or 300 r to 500 r weekly, total five times in fractionated exposure or 15 r to 100 r daily for 80 to 185 times in continuous fractionated exposure. One eye only of each animal was irradiated, the other serving as a control.

Clinical examination and determination of minimal dose of cataractogenic level

The eye was examined monthly under oblique illumination with the slitlamp over a period of 60 to 349 days. The minimal amount of X-ray exposure causing lens opacities was determined by the histologic findings in the lens compared with the control eyes. By this method it is possible to determine with a fair degree of certainty whether the radiation cataract will or will not occur in the future.

Results of minimal cataractogenic dose

From Table 1 it can be seen that the minimal dose of cataractogenic level is 900 r and that of the epilation dose is 1,000 r, that is, the epilation dose is larger than that of cataractogenic dose (Rabbits 8 to 14).

As to the histologic findings as contrasted with the incubation period of X-ray cataract, the group with the irradiation dose of 1,000 r shows no pathologic findings in the lens at 60 days following exposure but there are cataractogenic changes after 160 days. Under 800 r there are no changes even after 313 days. On the other hand, in the large-dose groups, such as 1,300 to 1,500 r, the lens shows a clear evidence of cataractogenic changes even after 40 or 60 days.

Histologically, the incubation period varies inversely with the dose (Rabbits 6, 7, 11, 15, 19, and 26). Judging from 900 r group (Rabbits 7, 8, 9, 10) histopathologic incubation can be decided 160 days following irradiation. If there is no histologic change in the lens, there is no occurrence of radiation cataract. Therefore, the cataractogenic dose level is very distinct and there is no doubt about the result. However, this result seems to ap-

TABLE 1

MINIMAL CATARACTOGENIC DOSE WITH SINGLE EXPOSURE

Rabbit	Exposure Dose Observation	Period (days)	Clinical Findings		Histologic Epilation	
			Golden Yellow Reflex	Tuftlike Opacity	Findings	
1	600 r	225	—	—	−	−
2	600 r	243	—	—	−	−
3	700 r	258	—	—	−	−
4	700 r	314	—	—	−	−
5	800 r	263	—	—	−	−
6	800 r	313	—	—	−	−
7	900 r	60	—	—	−	−
8	900 r	162	—	—	+	−
9	900 r	254	—	—	+	−
10	900 r	262	—	—	+	−
11	1000 r	60	—	—	−	+
12	1000 r	233	—	—	+	+
13	1000 r	247	224	—	++	+
14	1000 r	312	295	—	++	+
15	1300 r	60	—	—	+	+
16	1300 r	202	198	—	++	+
17	1300 r	218	223	—	++	+
18	1300 r	247	199	242	++	+
19	1500 r	40	—	—	+	++
20	1500 r	199	167	183	++	++
21	1500 r	216	178	216	++	++
22	1500 r	309	188	226	++	++
23	1700 r	209	140	172	++	+++
24	1700 r	303	122	158	+++	+++
25	1700 r	366	147	169	+++	+++
26	2000 r	154	71	95	++	+++
27	2000 r	167	89	108	+++	+++
28	2000 r	198	104	149	+++	+++

ply only to rabbits at three to four months of age, whose X-ray exposure was 80 kv., added filter 2.0 mm. Al.

Similar experiments with a single exposure were carried out on three-month-old rats whose irradiation factors were the same as the rabbits: under 600 r there was no cataractogenic evidence even histologically but at 800 r the lens showed radiation cataract clinically after 265 days without epilation; while over 1,000 r there was more or less epilation, with radiation cataracts after the long period of incubation—almost the same results as with rabbits.

To obtain the results of minimal lethal doses at cataractogenic levels in fractioning exposures the experimental rabbits were divided into three groups: *Group A*, exposures twice a week, total 10 times, each dose was 150 r to 350 r; *Group B*, once a week, total five times, each dose 300 to 500 r; *Group C*, continuous fractionated exposure daily, each dose 15, 60, and 100 r for 80 to 185 days.

The results of Groups A, B, and C are shown on Table 2.

Group A. In the 150 r, 10 times group, the lens showed no evidence of cataractogenic changes clinically or histologically after 106 to 283 days. There was no epilation either. On the 250 r, 10 times group, there was slight epilation after 45 days and disappearing in a month. The lens appeared to have cataractogenic changes 60 days after the exposure on histologic examination; clinically in 199 to 224 days. On the 350 r, 10 times group, the lenses were clouded in 127 to 149 days revealing marked changes histologically.

Group B. In the 300 r group (total 1,500 r) there was neither sign of epilation nor histologic changes of the leps after 60 days, though lens opacities occurred after 215 to

230 days and severe changes of radiation cataract were observed on histopathologic examination. In the 400 r group (total 2,000 r), the rabbits show slight epilation at the lid margin as well as lens changes histologically in 60 days, and revealed radiation opacities after 150 to 194 days. In the 500 r group (total 2,500 r), there was marked epilation on the whole area of exposure, as well as cataractogenic changes of the lens histologically in 60 days.

The postcortical lens radiation opacity appeared clinically in 132 to 137 days and the anterior subcapsular opacity in 249 days.

Group C (continuous fractionated exposure daily, each dose being 15 r to 100 r, during 80 to 185 days). In the 15 r group daily for 185 times, there was no change to the lens. In the 60 r group daily for 180 times, there were no cataractogenic changes in the lens histologically at 130 days after the last exposure.

Comment

To determine the threshold level of the cataractogenic radiation dose the same age group of experimental animals must be used; otherwise, inconsistent and confusing results will be obtained. This is because younger tissue is more sensitive to irradiation than older tissue. My experiments were done on three-month-old rabbits exclusively so that the value of the threshold level of radiation cataract is constant. This technique facilitated the experiment so markedly that the results were excellent, determining the threshold level sharply and distinctly.

The experimental results (tables 1 and 2) show that a single large dose of exposure is more harmful to the lens than a fractionated

TABLE 2

Minimal cataractogenic dose with fractionated exposures

Rabbit	Exposure Dose Observation	Period (days)	Clinical Findings		Histologic Epilation	
			Golden Yellow Reflex	Tuftlike Opacity	Findings	
		Group A (Twice a week total 10 times)				
29	150 r×10	106	—	—	−	−
30	150 r×10	239	—	—	−	−
31	150 r×10	283	—	—	−	−
32	250 r×10	60	—	—	+	+
33	250 r×10	259	199	248	++	+
34	250 r×10	279	224	252	++	+
35	350 r×10	198	149	163	++	+
36	350 r×10	216	149	185	++	+
37	350 r×10	217	127	155	++	+
38	350 r×10	349	137	163	++	+
		Group B (Once a week total 5 times)				
39	300 r×5	60	—	—	−	−
40	300 r×5	258	230	255	++	−
41	300 r×5	285	215	239	++	−
42	400 r×5	60	—	—	+	+
43	400 r×5	160	150	—	++	+
44	400 r×5	154	142	—	++	+
45	400 r×5	194	150	179	++	+
46	500 r×5	60	—	—	++	++
47	500 r×5	102	—	—	++	++
48	500 r×5	216	132	167	++	++
49	500 r×5	312	137	171	+++	++
		Group C (Daily exposure)				
50	15 r×185	314	—	—	−	−
51	60 r×130	261	—	—	+	−
52	100 r× 80	200	175	200	++	+

one. With a single exposure, the threshold dose of cataractogenic level is 900 r, while in fractionated ones, that is, twice a week total 10 times (1,500 r to 3,500 r) no lens change is revealed in the 1,500 r group; while irradiation once a week, total five times in a group receiving the same dose (1,500 r) the lens appeared histologically to have cataractogenic changes. With daily exposure, there is no harm in 15 r radiation while over 60 r is very dangerous to the lens, threatening development of radiation cataract.

The threshold dose of cataractogenic level does not depend upon the total sum of radiation but upon the manner of irradiation. With fractionated exposure at the same total dose over an equal radiation period, the smaller the dose at each exposure the less harm to the lens.

Regarding the recuperative power of the lens as compared to other tissue, Birch-Hirschfeld[14] and Rohrschneider[15] reported that the lens is disturbed far more easily because its recuperating power is weaker than that of other tissue. Although the lens also has an accumulating tendency, as have other tissues, the cataractogenic dose is always lower than that of the epilation one. It is reported by Rohrschneider that the epilation dose is double with fractionated irradiation but the cataractogenic minimal dose is almost equal to the dose given at a single exposure, suggesting that the lens has a larger accumulating power than other tissue.

It appears, however, that the lens has almost the same recovery function as other tissue because both the epilation dose and the cataractogenic dose are almost double with fractionated radiation than with the single exposure, when each dose is small (such as under 150 r). My experiment shows that the minimal cataractogenic and epilation doses are 900 r and 800 r with single exposure and over 1,500 r with the fractionated exposure of 150 r doses twice a week 10 times. However, the result is different when each dose is 300 r once a week to a total 1,500 r; this is a cataractogenic dose. According to Sinsky reporting the atomic-bomb cataract, 84 percent of the patients who had epilation after the raid developed radiation cataracts. This suggests that the epilation dose is almost equal to the cataract dose in atomic-bomb radiation.

My single-exposure results are almost the same as those reported by Rohrschneider,[1] that is, 890 r with 188 kv. add filter 0.5 mm. Cu and 3.0 mm. Al and 980 r add filter 3.0 mm. Al only. The minimal dose for the cataractogenic level of Peter[2] was 550 r with 150 kv., and that of Cogan,[6] 250 r for X rays, appears too low.

The results of continuous fractionated radiation are far more important to workers in X-ray laboratories and atomic energy factories. Under 60 r daily exposure is not cataractogenic but exposures over this amount may produce radiation cataract.

Although, in the minimal dose of the cataractogenic level, there are some differences between the animal species, such as between rabbits and rats, the differences are not marked. They may be due to differences in the size of the eyeball. The distance from the surface to the lens is longer in rabbits than in rats, the one is about 8.0 mm. while the other is about 3.0 mm., decreasing the amount of X-ray dosage reaching the lens of rabbits to 70 percent at 80 kv., while, in rats, 90 percent reach the lens. The softer the ray, the greater is the decrease; the harder the ray, the smaller. It would seem necessary, in order to determine the minimal lethal dose of cataractogenic level to study various kinds of X rays; such, however, is not the case because the wavelength itself does not influence the roentgen effect. When the dose of one type of X ray is measured by the isodosen curve, the information can be applied to other types.

Summary

1. Lens changes resulting from irradiation have a critical dose level, using the same fac-

tors, for animals or humans in the same age groups.

2. The minimal dose of cataractogenic level may be determined by histologic findings only, 160 days following exposure, and not on the basis of clinical symptoms.

3. The factors employed are 80 kv., added 2.0 mm. Al filtration, 12 cm. target skin distance and 600 r to 2,000 r in single exposure or 150 r to 350 r twice a week total 10 times and 300 r to 500 r once a week total five times in fractionated exposure, or 15 to 100 r, 80 to 185 times in continuous fractionated exposure.

The results are: minimal cataractogenic doses are 900 r in single exposure, over 150 r ×10 (1,500 r) at twice a week, and under 300 r ×5 (1,500 r) once a week in fractionated exposure, and under 50 r daily in continuous fractionated exposure. Minimal cataractogenic doses are always lower than epilation doses. Lens has almost the same recovery power to the X-ray radiation as other tissues.

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LAMELLAR UNDERMINING*

A PRELIMINARY REPORT ON A TECHNIQUE OF SCLERAL BUCKLING FOR RETINAL DETACHMENT

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With the recent development of retinal detachment surgery there has been a trend toward scleral resection in one form or another, especially for complicated cases. Such cases are those occurring in severe myopia with multiple tears, in massive detachments where no retinal tears can be found, in elderly subjects with multiple tears in an atrophic retina, in retraction of the vitreous after vitreous hemorrhages, in long-standing detachments, and as a secondary procedure after previously unsuccessful retinal detachment surgery.

While Müller[1] devised the procedure of complete scleral resection for shortening the globe in 1903, it was Lindner[2] who popularized it in 1933. However, the procedure presented some difficulty in technique because of the danger of rupture of the choroid and loss of vitreous.

In 1949, Dellaporta[3, 4] made an important contribution by introducing a modification of this scleral shortening process. Instead of removing the complete thickness of the sclera, he merely removed the outer layer as a lamellar resection and then sewed the two edges of the wound together, thus producing a scleral buckling.

It is interesting to note that in 1917, Torok, following a procedure devised by Blaskovicz, removed a superficial scleral lamellar section and placed sutures in the remaining scleral edges. However, he then cut through the remaining deep layer of sclera at its posterior border to expose the choroid, and separated the deep scleral layer from the choroid and treated the choroid before tying the sutures. During the tying he tucked in the deep remaining scleral flap between choroid and the shortened outer scleral coats. This procedure, of course, exposed the eye to the same difficulties as did Lindner's complete resection. Dellaporta's procedure, on the other hand, was much safer and easier of execution and met with some degree of popularity. Dellaporta's procedure was further developed by Paufique and Hugonnier,[5] as well as Shapland.[6]

Recently, Schepens,[7] in the course of his extensive work in this field, added a modification to this technique of lamellar resection with buckling by introducing a polyethylene tube in the groove where the lamella had been resected, thus producing an even more pronounced buckle and providing a rather sharp line of defense against detachment of the retina posterior to the buckle.

All these methods shed new light and hope on the management of the complicated retinal detachment cases, and only the future will tell the full value of these procedures.

While the use of a polyethylene tube seems to fulfill its purpose and is reported to cause hardly any untoward foreign body reaction, it still seems desirable to accomplish a similar effect, if possible, without the use of a foreign body. For this reason, one of us (M. C.), devised the procedure about to be described.

PROCEDURE IN PATIENTS

Four patients were operated on in the manner to be described. All of them had a high degree of myopia with large tears, and all had had previous surgery which had been unsuccessful.

In all four cases, the eye was prepared in the usual manner and the scleral surface exposed after undermining conjunctiva and

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tenotomizing the appropriate recti muscles (fig. 1). In each of the cases, a lamellar strip was outlined with a No.-15 Bard Parker blade, very much like the original lamellar section described by Dellaporta.[4] The anterior incision of this strip was 13 mm. from the limbus and the posterior one between 17.5 and 18 mm. from the limbus. Its length was about one-third the circumference of the globe in two of the cases, and one-half the circumference of the globe in the two others. Thereafter, the incisions were carried deep, until the dark choroid could be seen showing through the thin inner layer of the sclera. At this point, each edge of the lamella was undermined for a distance of about 1.5 mm. toward the middle of the strip, leaving the lamella attached to the sclera along a one-mm. central strip.

When the undermining had been carried out on either edge, it was found that the lamellar strip had contracted somewhat upon itself (fig. 2) and curled in a direction opposite to the original scleral curve, thus forming a cordlike band about 1.5 mm. in thickness, instead of the thin, flat, 5.0-mm. strip it had originally been.

Thereafter, 4-0 black silk sutures were placed through the intact edges of the exposed scleral wall on either side of the lamella at two- or three-mm. intervals and left untied. Partially penetrating diathermy punctures were then laid down on either side of the lamellar strip in the deep layers of the exposed sclera, very much as described originally by Dellaporta. Thereafter, some partially penetrating cautery was laid down in the region of the tear. Fluid was then released by laying down a small ring of cautery in the area where most of the fluid was thought to have accumulated, and a beveled No.-19 gauge hypodermic needle was inserted in the uncauterized area inside the ring of cautery to release this fluid. This technique of releasing fluid without the simultaneous use of cautery was found to be preferable because, in many cases, penetration with cautery caused enough coagulation to block the escape of subretinal fluid.

The release of fluid was considered a very

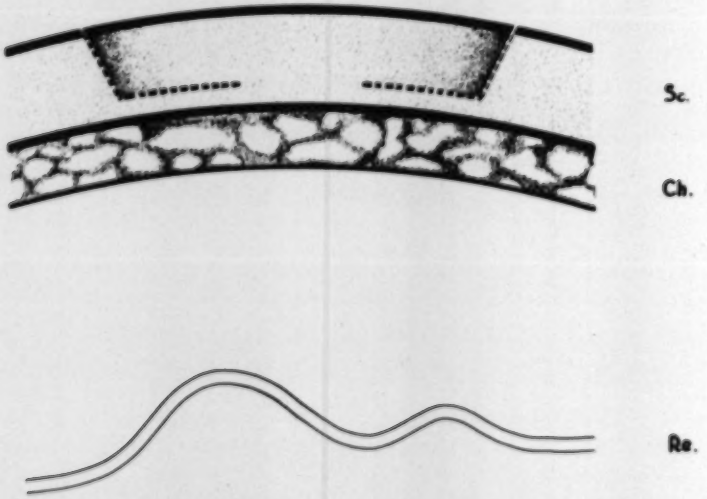


Fig. 1 (Chamlin and Rubner). Schematic diagram showing cross-section through the area of sclera to have lamellar undermining and scleral buckling.

Sc = sclera Ch = choroid Re = retina

Parallel, broken lines show incisions through outer layer of sclera, with undermining of 1.5 mm. on either side, leaving the scleral lamella intact in its original attachment along a 1.0-mm. strip throughout its length.

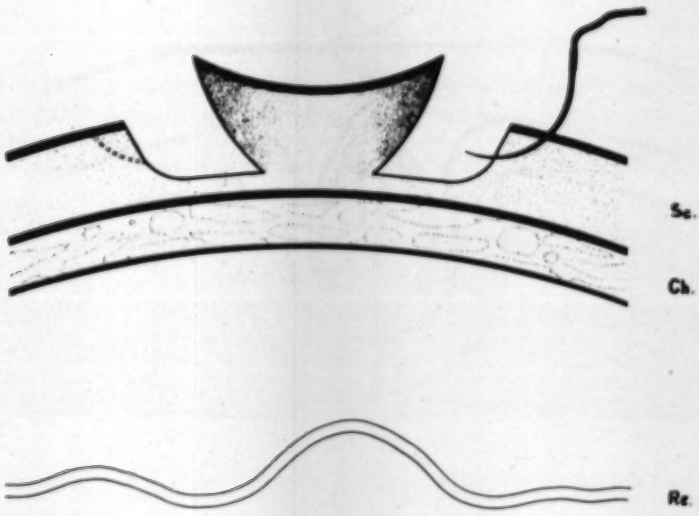


Fig. 2 (Chamlin and Rubner). After undermining, the strip contracts and curls on itself, so that the original, thin, 4.5 or 5.0 mm. scleral lamella becomes a narrow, cordlike strip, lying in the center of the groove, where it retains its original attachment to the deeper layer of sclera. The needle is shown going through one edge of the scleral groove, and parallel broken lines show the site for the other bite to be taken with the same needle.

essential part of this procedure, not only for the usual reason of helping the retina to make contact with the cauterized choroid but also to soften the globe sufficiently to allow easy approximation of the scleral edges without tearing through of the sutures.

While the scleral edges were being approximated in the softened globe, the assistant used an iris spatula to depress the undermined scleral strip, holding it below the surface of the scleral edges being approximated and withdrawing the iris spatula gently as the black silk sutures were pulled taut. Thus, the partially undermined scleral lamella was buried completely in the buckle, and helped to create this pronounced buckle.

When all the sutures had been securely tied, it was found that the previously rounded contour of the globe had become flattened (fig. 3) and the buckle was easily seen in the fundus. Several other partially penetrating diathermy punctures were then laid down on the opposite side of the sutures, two or three mm. away from them and at the same distance apart, very much as described by Dellaporta.

In the fourth case, before outlining the lamella, we laid down a single line of partially penetrating cautery punctures in a line that was later to become the middle of the scleral lamella. Thus, an extra line of cautery punctures was created right at the buckle, and this line on the scleral surface served as a landmark of the middle of the scleral lamella to be outlined.

The patients were kept in bed from five to eight days, and allowed to go home at the end of 10 to 14 days.

In all four patients, a good buckle was visible postoperatively, and the retina was in good position. In two of the cases, detachment recurred; in one case after four weeks and, in the other case, after six weeks. In the former, the new detachment took place in another area. In two others of the four cases, the retina is still in excellent position, one after six weeks and the other after four weeks.

Animal procedures

In order to visualize what happens to the sclera anatomically, parts of this procedure

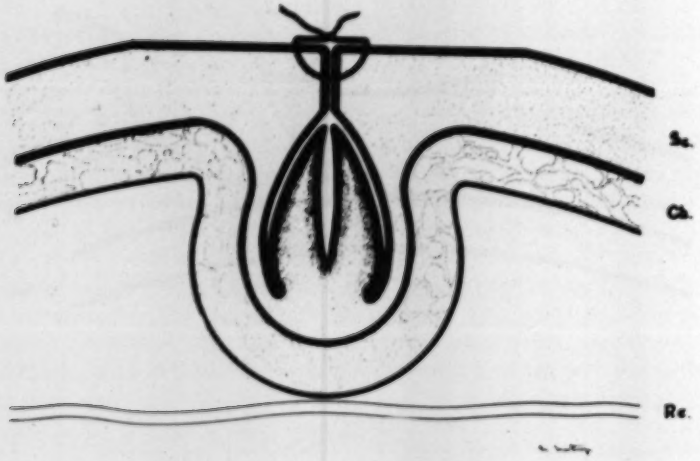


Fig. 3 (Chamlin and Rubner). Section through one of the tied sutures, showing the buckle produced by the approximation of the two scleral edges bounding the scleral groove. The undermined lamella has contracted on itself into a cordlike mass and helps to create a more firm and pronounced buckle to approximate the retina. The various cut scleral surfaces approximating one another in this buckled tissue create suitable conditions for firm adhesions in this buckle.

Note the flattening of the original scleral curvature in the area of the buckle.

were carried out on eight dark-gray rabbits, each weighing between 2,200 and 3,300 gm. Intravenous Nembutal was used for anesthesia. Since the purpose of the animal work was merely to observe the buckling of the sclera, no attempt at diathermy punctures was made.

It was found that the rabbits' sclera was quite thin and thus presented technical difficulties in producing a good, thick scleral lamella. Therefore, in several of the eyes, not only did choroid present but vitreous was lost. However, in those rabbits' eyes with which we were successful, a 3.0- to 3.5-mm. strip was made for a length from 15 to 20 mm., and aqueous was subsequently released from the anterior chamber in order to soften the globe and allow easy tying of the black-silk sutures. We were successful in producing a good buckle without any untoward complications in four of these eyes. In another eye, a complete lamellar resection was made and, following the general technique of Schepens, a one-mm. polyethylene tube was inserted in the lamellar groove and the sutures tied over this tube.

The rabbits were killed at different stages up to 14 days postoperatively, when the globes were opened for gross inspection of the buckle. Histologic sections of these buckles were then made. One of the better ones is shown in Figures 4 and 5. The section of the buckle produced by the polyethylene tube is shown in Figures 6 and 7, the tube having been removed before embedding and sectioning.

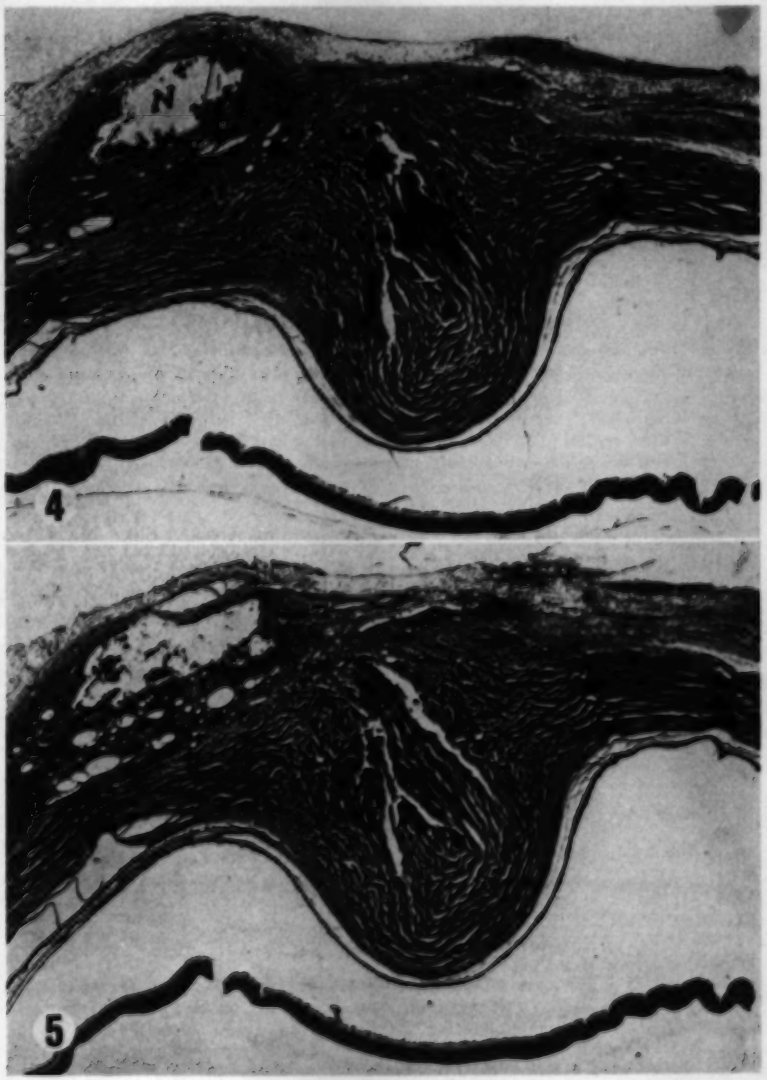
Comment

In view of the intense cellular reaction encountered about the silk sutures, we are considering other suture material, such as nylon.

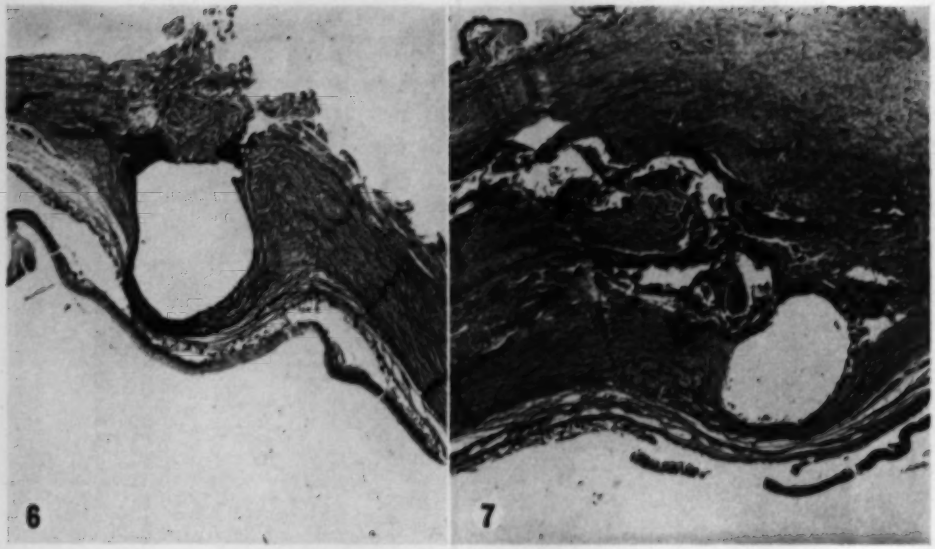
Although all four of the cases reported had been operated on previously, the sclera encountered was in good enough condition to allow the production of the undermined lamella. However, it is conceivable that in some cases in which previous surgery had been performed, a thin, necrotic sclera may be encountered, and would be unsuitable for lamellar undermining in this area.

This report is not intended as a study of

the efficacy of scleral shortening operations, nor is it meant to show any conclusive advantage over any of the procedures in current use. Further clinical study and more extended observations in animals are being planned for these purposes. However, even in this early stage, "lamellar undermining," which we believe an appropriate name for this procedure, seems to offer several advantages. The surgical procedure is a bit



Figs. 4 and 5 (Chamblin and Rubner). Sections through buckle in right eye of Rabbit 5. The eye was removed eight days postoperatively and the sutures were removed prior to embedding in paraffin. The buckle is quite pronounced and the approximated surfaces show evidence of firm fibroblastic union, particularly across the outer scleral edges. N = area of necrosis produced by silk suture in Figure 4. A similar area is seen in Figure 5.



Figs. 6 and 7 (Chamlin and Rubner). Section through buckle of left eye of Rabbit 4, also removed eight days postoperatively. A polyethylene tube had been inserted but removed prior to sectioning on the microtome, leaving the large, clear space in the buckle. In Figure 6, the scleral fibers around the space left by the tube show very little reaction but the union of the outer scleral layers is not very firm. In Figure 7, there is more episcleral tissue thickening over the site of the polyethylene tube, with irregular areas of adhesion between the two outer edges.

tedious, but not particularly difficult of execution. It utilizes, in part, Dellaporta's principle of lamellar resection, with its advantages of safety. It further utilizes Schepens' principle of adding some bulk to the folded, deep sclera. The bulk, however, is produced by the undermined scleral lamella itself. The undermining allows the lamella to contract into a thickened, cordlike mass, suitable to help such folding. It is believed that the raw scleral surfaces tend to help scar formation in the folded state, with less tendency to unfold. The retention of the middle strip helps to provide good vascularization for such scar formation.

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PATHOLOGY OF EXPERIMENTAL PRIMARY HERPETIC KERATITIS IN RABBITS*

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In adult man herpes-simplex virus infection of the outer eye characteristically produces a superficial keratitis with corneal hypesthesia, vesiculation of the epithelium, dendritic ulceration, and conjunctivitis. In children, after infection of the cornea with the same virus there develops a much more severe clinical picture which is considered to be the primary reaction of an individual who lacks antibodies. Hall, McKneson, and Ormsby[1] have shown that in experimental keratitis in rabbits, the clinical picture and antibody production are similar to those in man: After primary or initial infection of the rabbit cornea a severe keratitis develops —resembling the primary reaction to the virus in children; however, following the second inoculation on the same cornea the changes are only slight—as in characteristic dendritic keratitis in adult man.

Since the clinical picture of human primary herpetic keratitis is similar to that of rabbits, we studied the histopathology of experimental primary herpetic keratitis in rabbits employing a silver carbonate staining technique of del Rio Hortega.

Method

The virus used in this study was "Herpes Simplex Armstrong 1166" lyophilized in mouse brain and horse serum saline.† The virus was passed through Swiss mice three to seven times and was scratched into 32 corneas of normal rabbits under pontocaine anesthesia with a No.-18 hypodermic needle.

The clinical course of the inoculated eyes was as follows:

For the first three to four days following the scratchings corneal clouding developed. From five to 10 days, in approximately 80 percent of the eyes, typical dendritic figures as stained with two-percent fluorescein dye were found. After 18 to 20 days, 90 percent of the eyes had healed leaving superficially vascularized scars. In the remaining 10 percent of the eyes the corneal disease exacerbated and severe clouding of the cornea and pericorneal irritation were noted, but there was no deep ulceration or perforation. Twenty-five of the eyes received no antibiotics while the others were treated with chloromycetin (Chloroamphenicol) ophthalmic drops (0.5 percent, four times daily). The course of the disease was not influenced by this treatment (compare Coles-Carenini and Cambiaggi[2]).

Eyes with symptoms of herpetic infection were enucleated 12 to 14 days after inoculation. The corneas were fixed immediately in bromformol (Cajal solution). Meridional and surface-parallel sections were made on the freezing microtome and stained with hematoxylin-eosin, with floxin-tartrazine (Lendrum[3]), and with the "panoptic silver carbonate method" of del Rio Hortega.[4] The latter has proved to be very successful in demonstrating the intricate structures of the cornea (Prieto Diaz,[5] Scharenberg,[6] Sverdlick,[7] Wolter,[8] Wolter and Shapiro[9]).

Histologic description

Four eyes from different rabbits were examined which at the time of enucleation showed clinically a marked keratitis. The histologic picture was fundamentally the same in all corneas.

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† Virus was supplied by Dr. Thomas Francis, Virus Laboratory, School of Public Health, Ann Arbor, Michigan.

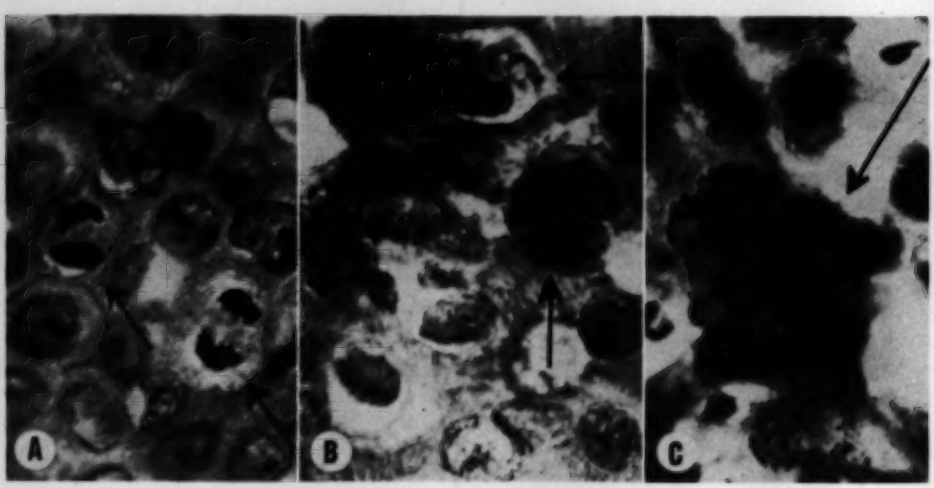

Fig. 1 (Wolter, Shapiro, and Whitehouse).
(A) Two mitotic figures in a surface-parallel section of the corneal epithelium of a rabbit with herpetic keratitis.
(B) Swollen and deformed nuclei of epithelial cells of the same cornea.
(C) Epithelial giant cell of the epithelium of the same cornea.
(A, B, and C: Hematoxylin-eosin, ×1,000.)

The epithelium of the corneas showed typical changes:

There was a marked increase of mitotic figures in some areas (fig. 1-A), while in others there was vacuolization, irregular swelling, and deformation of the nuclei and multinucleation (giant-cell formation) (fig. 1-B and C). Mitoses and nuclear changes were clearly visible in both silver carbonate and hematoxylin-eosin preparations. There were also typical intranuclear inclusion bodies in many epithelial cells which were demonstrated by the floxin-tartrazine method of Lendrum.[3]

Necrosis of epithelial cells was common and resulted in vesiculation of the deeper layers of the affected areas. Some of the vesicles were confluent and formed large bullae (fig. 2). The membrane of Bowman was still preserved in some of them and formed the base of the bullae (fig. 3-A).*

Frequently, however, all structures of the damaged epithelium were destroyed completely resulting in ulcer formations which extended into the infiltrated outer layers of the stroma (fig. 3-B).

We were unable to impregnate the nerve fibers of the corneal epithelium and the subepithelial nerve plexus. Probably, both were destroyed.

The keratitis was not limited to the epithelium but extended into the stroma of the cornea—particularly into its outer layers. The pathologic changes were composed of:

1. Degeneration and proliferation of the fixed cells of the cornea.
2. Degeneration of the lamellae.
3. Immigration of leukocytes and lymphocytes.
4. Immigration of fibroblasts.
5. Superficial vascularization.
6. Degeneration of the nerves.

1. *The fixed elements of the outer layers* of the corneas were partly necrotic and many were destroyed. In the deeper layers these cells were star-shaped and hypertrophic; the nuclei were blurred, the cystoplasm was argentophilic and the normally straight

* Our findings confirm the report of Yamamoto[10] who first described the membrane of Bowman in the cornea of rabbits.

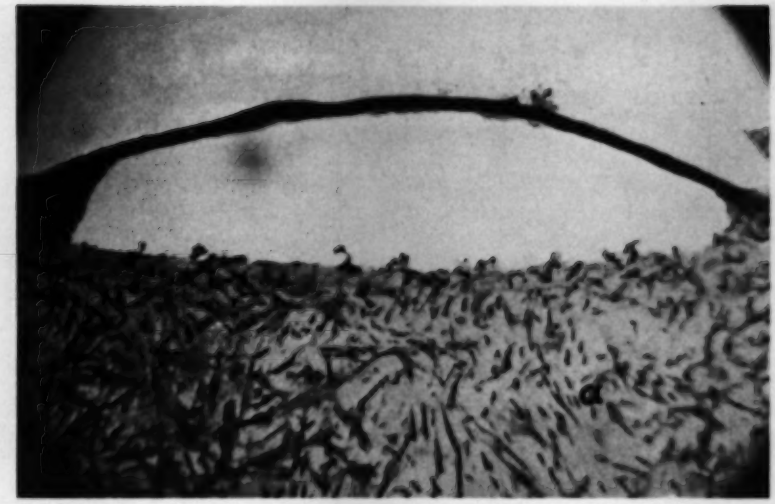

Fig. 2 (Wolter, Shapiro, and Whitehouse). Bulla of the epithelium in herpetic keratitis of a rabbit. The corneal stroma (a) is densely infiltrated with fibroblasts, leukocytes, and lymphocytes. (Meridional section, Hortega method. ×200.)

processes of the cells formed a dense, irregularly intertwined network (fig. 4). The fixed elements of the posterior layers of the stroma showed either slight reactive changes or were normal.

2. *The normally straight lamallae* of the outer layers of the corneal stroma were swollen, wavy, and only faintly impregnated (figs. 4 and 5). The lamellae of the deeper layers were normal.

3. *There was a dense infiltration with leukocytes and lymphocytes* in the outer layers of the stroma—especially in the areas of ulceration (fig. 6-A). The inflammatory

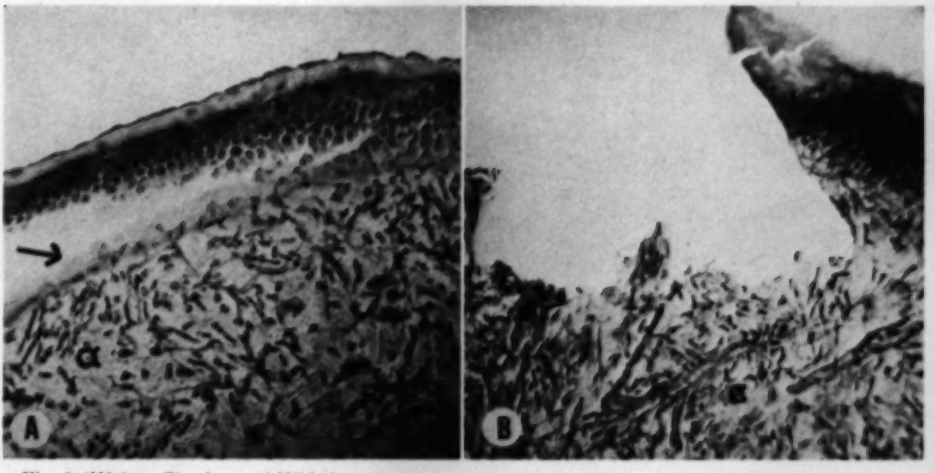

Fig. 3 (Wolter, Shapiro, and Whitehouse).

(A) Part of a bulla of the epithelium in herpetic keratitis of a rabbit; Bowman's membrane (arrow) is still visible. Dense infiltration of the corneal stroma (a). (Meridional section, Hortega method ×200.)

(B) Epithelial ulcer, the base of which is formed by infiltrated corneal stroma (a). (Meridional section, Hortega method. ×200.)

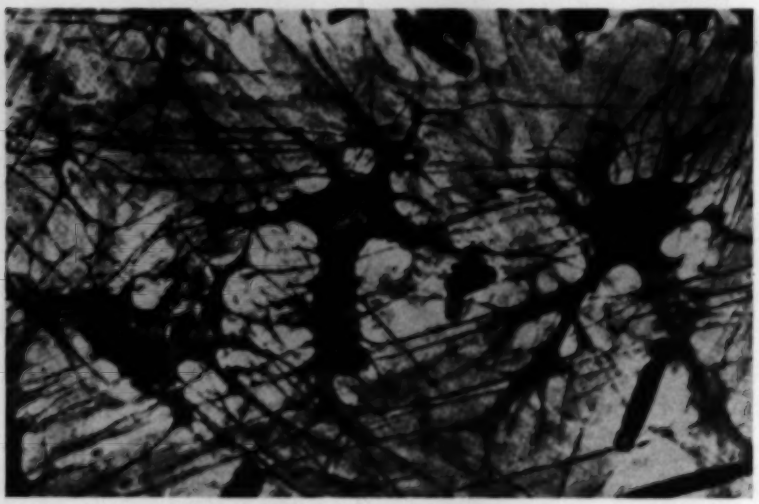

Fig. 4 (Wolter, Shapiro, and Whitehouse). Hypertrophic, star-shaped fixed cells of the middle layers of a cornea of a rabbit with herpetic keratitis. The processes form a dense network of fibers. (Surface-parallel section, Hortega method. ×800.)

cells were arranged in the direction of the fibers of the lamellae and formed parallel interlacing rows. There was no infiltration in the posterior layers of the stroma. Often, single lymphocytes were seen within the cytoplasm of hypertrophic fixed elements (fig. 5).

4. *In the outer layers of the stroma* the ulcers were surrounded by many spindle-shaped fibroblasts which immigrated from the limbus (fig. 6-B).

5. *In all four cases there was superficial vascularization of the cornea.* Figure 7 demonstrates branching solid aggregations of endothelial cells representing primitive

Fig. 5 (Wolter, Shapiro, and Whitehouse). Lymphocyte within the cytoplasm of a hypertrophic fixed cell (arrow) in herpetic keratitis of a rabbit. (Surface-parallel section, Hortega method. ×800.)

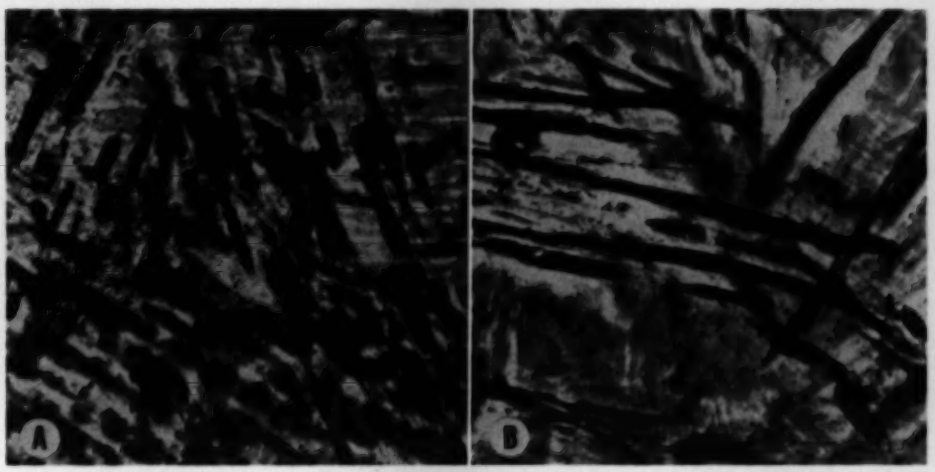

Fig. 6 (Wolter, Shapiro, and Whitehouse).

(A) Surface-parallel section of the outer layers of the corneal stroma in the area of ulceration in herpetic keratitis of a rabbit. Infiltrating the leukocytes and lymphocytes arranged in the interlacing pattern of the fibers of the corneal lamellae. (Hortega method. ×800.)

(B) Immigrated fibroblasts in the outer layers of the corneal stroma in the area of the ulcers. (Surface-parallel section, Hortega method. ×800.)

vessels. There was no deep vascularization of the cornea.

6. *All nerve bundles of the stroma* were severely damaged. Most fibers had disappeared and only the nuclei of the cells of Schwann survived. There were scattered delicate newly formed nerve fibers with numerous alternating swellings in the degener-

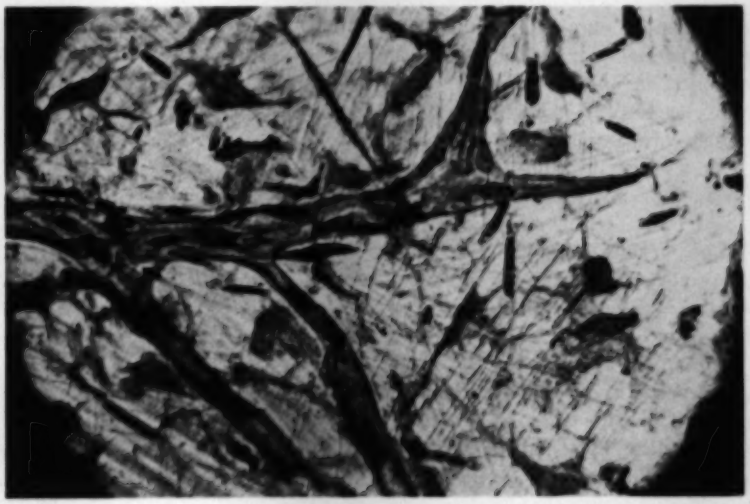

Fig. 7 (Wolter, Shapiro, and Whitehouse). Primitive lumenless vessel growing into the outer layers of the corneal stroma in herpetic keratitis: superficial vascularization. (Surface-parallel section, Hortega method. ×200.)

Fig. 8 (Wolter, Shapiro, and Whitehouse). Broken-down nerve bundle of the corneal stroma in herpetic keratitis in rabbit (a). The nuclei of the Schwann-cells have survived. Some newly formed nerve fibers with swellings and an irregular course (b). (Surface-parallel section, Hortega method. ×500.)

ated nerve bundles (fig. 8).

The membrane of Descemet and the corneal endothelium were normal (fig. 9).

Discussion

The occurrence of numerous mitotic figures in the epithelium of the cornea is a relatively common phenomenon which has been described in healing of corneal wounds[11] and in normal cornea following removal of Harderian and lacrimal glands.[12] This observation was quite evident in all four of our cases and indicates extensive regeneration of epithelial cells in areas which apparently were not damaged by the infection.

Vacuolization, swelling, deformation, and abnormal division of the nuclei of epithelial cells were found in all four cases. These nuclear changes are known to exist in herpetic keratitis (Kimura and Thygeson[13]). Typical intranuclear inclusion bodies and "multinucleated epithelial cells" (the latter also called epithelial giant cells) as described above are considered to be the specific reactions of epithelial cells to the herpes-simplex virus.[14–17] In man these nuclear changes of epithelial cells are constantly seen in scrapings from dendritic keratitis.

The histopathologic picture of the ulcers is an equivalent of the dendritic figures seen

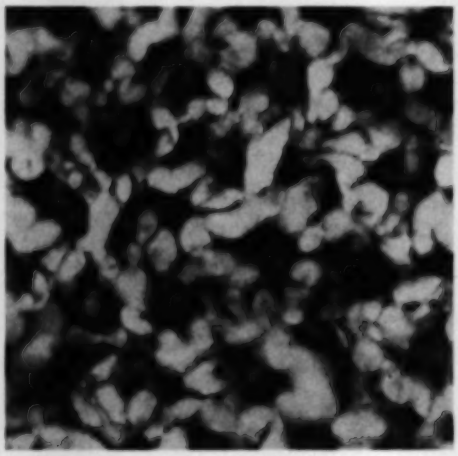

Fig. 9 (Wolter, Shapiro, and Whitehouse). Corneal endothelium of cornea of a rabbit with herpetic keratitis which shows no signs of damage or irritation (Surface-parallel section, Hortega method. ×800.)

clinically on the surface of the corneas after inoculation.

The histopathologic changes of the stroma of the cornea consisted of the reactions of five tissue elements, which are described above. The degeneration and proliferation of the fixed elements in herpetic keratitis are not specific, since similar reactions occur also following injury of the cornea in rabbits.[9] The accumulation of leukocytes, lymphocytes, and fibroblasts and the superficial vascularization of the outer layers of the cornea are also not specific. The macroscopic picture of the degeneration of nerve bundles in experimental primary keratitis in rabbits was described by Löwenstein[18] but we could trace no report of the histopathology of the nerves of the cornea in this condition. As already stated the nerve bundles throughout the cornea suffered very severe damage which was followed by a very limited regeneration at the time of enucleation (up to 14 days). We believe that these findings satisfactorily explain the hypesthesia constantly present in herpetic keratitis.

Summary

It is possible to demonstrate in detail the histopathologic changes in the cornea of rabbits following inoculation with herpes-simplex virus. In addition to the specific changes of the epithelium severe damage was suffered by the fixed cells and the lamellae of the outer layers of the corneal stroma. The extensive reactions in the outer layers were composed of infiltration with leukocytes, lymphocytes, and fibroblasts and of superficial vascularization. All nerves of the cornea were destroyed and there was only very limited regeneration 14 days after inoculation.

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FURTHER STUDIES OF THE EPISCLERAL VENOUS PRESSURE IN GLAUCOMA*

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The relationship between the intraocular pressure and the pressure measured in episcleral veins during variations of the intraocular pressure has been a matter of discussion. The technique and the type of episcleral veins chosen for these measurements have greatly influenced the results.

Thomassen[21-24] compressed ciliary veins of arterial type described by Heerfordt[10] in all cases where they could be found, otherwise he used the more common perforating veins at the point of their emergence from the sclera. He reported variations in the venous pressure preceding changes in the intraocular pressure, and venous pressure as high as 60 mm. Hg. These results were discussed by Goldmann.[8] Bain[2] reported effects of phasic variations of the intraocular pressure and of miotics on the pressure necessary to compress veins which could be seen to emerge from the sclera, but according to him variations in pressure could be detected in most of the episcleral veins near the limbus.

Löhlein and Weigelin[16] reported measurements of the pressure in perforating veins close to the point of emergence from the sclera and Löhlein[15] apparently using the same technique followed the venous and the intraocular pressure. He found after treatment with pilocarpine an initial rise in the episcleral venous pressure followed by a decrease back to about the normal level. Although it is not quite clear from the description which kind of veins were selected for measuring the venous pressure, it seems probable that different kinds of veins were used by Löhlein as compared to those used by Thomassen and Bain.

Thomassen, Perkins, and Dobree[25] reported briefly that the pressure in some aqueous and other episcleral veins was found to be about 5.0 mm. Hg in the diurnal phase of decreasing intraocular pressure. When the bulbar tension started to increase, the pressure in the aqueous and other veins and in small veins connected with the aqueous veins also increased and rose by degrees to 14 mm. Hg. No figures of the intraocular pressure were given. Rickenbach,[18] measuring the pressure in aqueous veins in cases of chronic simple glaucoma during increasing and decreasing phases of the intraocular pressure, found in some cases no change in the venous pressure and in other cases a slight change of a few mm. Hg.

Dobree[4] recorded the episcleral vessels by serial photographs during variations in the caliber of the episcleral veins. He suggested that the phase of vasodilation could play a part and perhaps an important part in reducing tension of whatever origin; and that the reduction of tension by miotics may be partly due to the fact that both pilocarpine and eserine, which are known to have a direct vasodilator effect on vessels, may reduce the pressure in the scleral and episcleral veins. Kleinert,[11] using a similar technique, reported the same type of variations of the caliber of the episcleral veins.

When the vessel is compressed the blood flow is arrested and the pressure gradient along the vessel is wiped out. The pressure measured at the point of compression is, therefore, higher than the normal pressure at the same point in the unobstructed vessel and reaches the pressure level which exists at the next proximally located junction with another vessel. By compressing perforating veins at the point of their emergence from

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the sclera, a pressure estimate is obtained which is somewhere between the real episcleral and the intrascleral of intrabulbar venous pressure. Seidel[20] discussed in detail the method of measuring the arterial and venous pressure in ocular vessels by compressing the vessel, and the errors, which all have, have a tendency to give an erroneously high value.

Seiedl reported a pressure of 10 to 14 mm. Hg, mostly about 11 mm. Hg, in the episcleral and anterior ciliary veins of normal human eyes. The upper value of 14 mm. Hg was mostly found in the ciliary veins of the type described by Heerfordt and sometimes a pressure of 15 mm. Hg was found in these veins. According to the new calibration scale approved by the American Academy of Ophthalmology and Otolaryngology (1954), the average intraocular pressure in normal human eyes is about 16 mm. Hg. This value is close to the pressure which Seidel found in the perforating veins.

When episcleral veins are used for pressure measurements, it is of importance to distinguish between the pressure in the episcleral veins themselves and the pressure which is required to compress and obstruct the flow in these vessels.

Therefore, by using the method of compressing the episcleral veins at the point of their emergence from the sclera as used by Thomassen and Bain, the true pressure in the episcleral veins themselves was not obtained. When a pressure chamber fitted with a transparent membrane is used, it is necessary to be certain that the rigidity of the membrane itself does not compress the vein. A cellophane membrane as used by Thomassen was shown to have a considerable rigidity, even when it was softened in water,[13] and might therefore influence the results.

The venous structure into which the aqueous vein empties is called a recipient vessel according to Ascher's terminology.[1] The aqueous vein and recipient vessel can be located in the conjunctival or in the episcleral layers. The purpose of the present study has been to follow the pressure in the recipient vessels or in regular conjunctival and episcleral veins, avoiding vessels with deep connections through the sclera, over a period of time during which wide variations of the intraocular pressure occurred. There is only a small pressure gradient along the aqueous veins as shown by measurements performed from the point where the aqueous vein emerges through the depth of the sclera to the recipient vessel (Goldmann;[7, 8] Linnér,[12, 13]) and the pressure in the network of regular episcleral and conjunctival veins is close to the pressure in the aqueous veins (Linnér, Rickenbach, Werner[14]). The apparent outflow pressure was found to be proportional to the intraocular pressure minus 11 mm. Hg (Goldmann[6]; Rickenbach and Werner[19]). This value of 11 mm. Hg is close to the pressure in the aqueous and episcleral veins which is in good agreement with the assumption that the real outflow pressure is the difference between the intraocular and the episcleral venous pressure.

Method

Patients with untreated glaucoma and high intraocular pressure were selected for the study. If an aqueous vein could be found the recipient vessel was chosen for the pressure measurements, otherwise a regular episcleral vein was used. Perforating vessels emerging from the sclera were avoided. The appearance of the conjunctiva over the place of measurement was normal.

All determinations were carried out with the patient in recumbent position and a topical anesthesia (Ophthaine, Squibb) was used. Triplicate measurements of the episcleral venous pressure were made with a pressure chamber previously described (Linnér[13]). The intraocular pressure was measured with a Mueller electronic tonometer and calculated according to the new tables of Friedenwald.[5]

After an initial measurement of the episcleral venous and intraocular pressure, the patients were given either miotics topically,

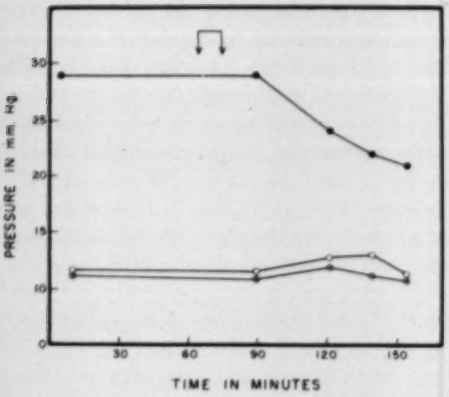

Fig. 1 (Linnér). *Case 1.* Chronic open-angle glaucoma. Solid circle: intraocular pressure. Open circle: pressure in episcleral vein. Dotted circle: pressure in recipient vessel. Arrow: instillation of two-percent pilocarpine, five drops during 10 minutes.

five drops during 10 minutes, or acetazoleamide (Diamox*) per mouth. The intraocular pressure and the episcleral venous pressure were then followed over a period of two to three hours.

Results and Discussion

Figures 1, 2, and 3 show the relationship between the episcleral venous and the intraocular pressure after instillation of two-percent pilocarpine, five drops during 10 minutes. Cases 1 and 2 had chronic open-angle glaucoma and Case 3 chronic narrow-angle glaucoma. In Case 1 a recipient vessel and a regular blood-filled episcleral vein were used for the measurement; in Case 2 a recipient vessel; in Case 3, where no aqueous veins was found, a regular episcleral vein.

Figures 4 and 5 show the same relationship in two eyes with chronic open-angle glaucoma after instillation of 0.25-percent eserine, five drops during 10 minutes. In Case 4 the venous pressure was measured in a recipient vessel, and in Case 5 in a regular

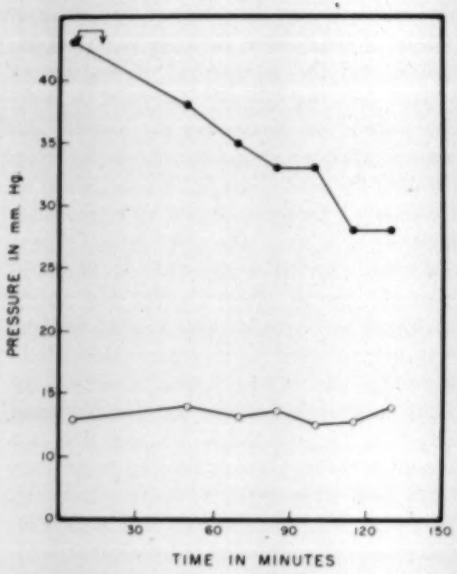

Fig. 2 (Linnér). *Case 2.* Chronic open-angle glaucoma. Solid circle: intraocular pressure. Open circle: pressure in recipient vessel. Arrow: instillation of two-percent pilocarpine, five drops during 10 minutes.

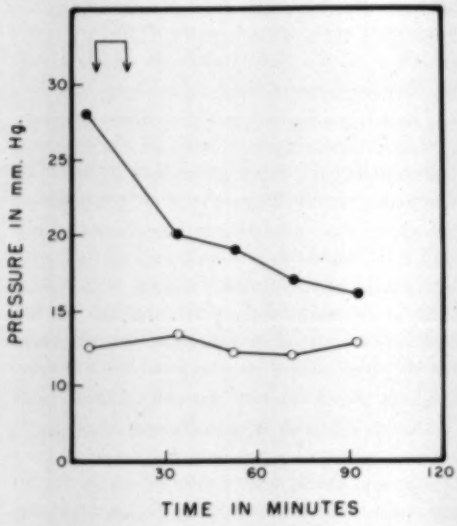

Fig. 3 (Linnér). *Case 3.* Chronic narrow-angle glaucoma. Solid circle: intraocular pressure. Open circle: pressure in episcleral vein. Arrow: instillation of two-percent pilocarpine, five drops during 10 minutes.

* The acetazoleamide (Diamox) used in this study was supplied through the courtesy of Dr. J. S. Gallagher of Lederle Laboratories Division, American Cyanamid Company.

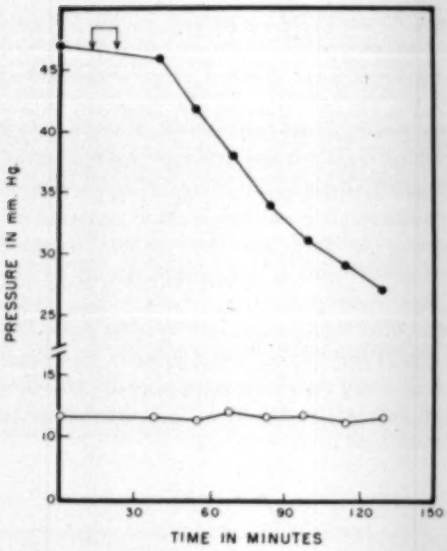

Fig. 4 (Linnér). *Case 4.* Chronic open-angle glaucoma. Solid circle: intraocular pressure. Open circle: pressure in recipient vessel. Arrow: instillation of 0.25-percent eserine, five drops during 10 minutes.

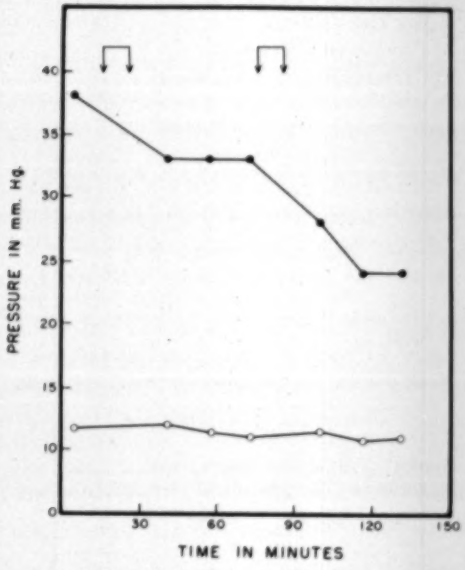

Fig. 5 (Linnér). *Case 5.* Chronic open-angle glaucoma. Solid circle: intraocular pressure. Open circle: pressure in episcleral vein. Arrow: instillation of 0.25-percent eserine, five drops during 10 minutes.

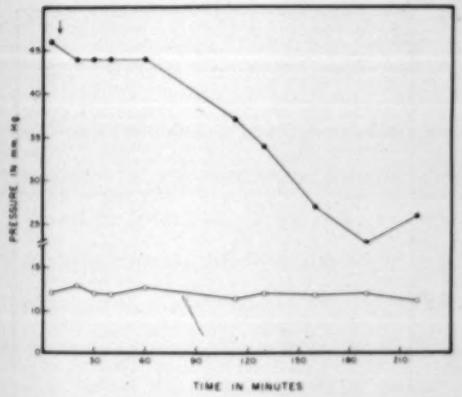

Fig. 6 (Linnér). *Case 6.* Chronic open-angle glaucoma. Solid circle: intraocular pressure. Open circle: pressure in episcleral vein. Arrow: 500 mg. Diamox by mouth.

episcleral vein because no suitable aqueous vein was found.

Figures 6 and 7 show the venous pressure in regular episcleral veins and the intraocular pressure in two cases of chronic open-angle glaucoma given acetazoleamide (Diamox) per mouth; Case 6 received 500 mg. and Case 7 received 750 mg.

A marked fall of the intraocular pressure was observed in all seven eyes. In Cases 1, 2, and 3, there is a slight apparent increase in episcleral venous pressure but this increase is not statistically significant. The standard error of a single determination as previously calculated[13] was found to be about 0.7 mm. Hg.

Miotics have been shown to cause an increase in coefficient of facility of outflow (C).[3, 9, 17] An increased outflow can be assumed, therefore, to have taken place in Cases 1 to 5 given miotics.

Assuming that the inflow of aqueous is constant, the excess volume of fluid which has to leave the eye in order to cause a certain fall in pressure can be calculated from Friedenwald's tables. Case 4, where the venous pressure was measured in a recipient vessel and the intraocular pressure dropped from 47 to 27 mm. Hg during two hours after instillation of eserine, will be taken as

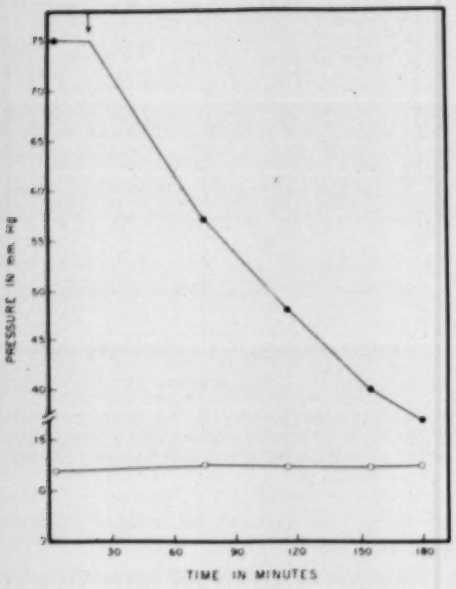

Fig. 7 (Linnér). *Case 7.* Chronic open-angle glaucoma. Solid circle: intraocular pressure. Open circle: pressure in episcleral vein. Arrow: 750 mg. Diamox by mouth.

an example. A volume of approximately 10 cu. mm. corresponds to this fall of 20 mm. Hg in intraocular pressure. This represents an excess outflow at the rate of 0.1 mm.^{3} per minute, a small fraction of the usual rate of flow. The stability of the pressure in the recipient veins and in the ordinary episcleral veins, when aqueous outflow is increased slightly by miotics or decreased markedly by acetazoleamide (Diamox), makes it clear that the pressure in these recipient veins is determined mainly by the local hemodynamics and is very little influenced by the dynamics of aqueous flow. The system behaves as if the aqueous was being discharged into a constant pressure chamber of such large capacity as to be insensitive to variations in aqueous flow.

Summary

The pressure in aqueous and regular episcleral veins was followed during a period of decrease in the intraocular pressure lowered by miotics or acetazoleamide (Diamox). No significant change in the venous pressure was found.

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MICRORADIOGRAPHIC STUDY OF THE INFLUENCE OF HYALURONIDASE ON THE PERMEABILITY OF THE INNER WALL OF SCHLEMM'S CANAL*

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One of us (J. M. Collette, 1953) demonstrated that, in men, after subcutaneous injection of a hydrosoluble contrast substance (Umbradil) the X-ray film shows a homogeneous opacity, which changes immediately into an image of reticular pattern, spreads in the beginning superficially, and diminishes afterward in intensity following the resorption of the contrast substance.

The previous or simultaneous injection of 0.5 mg. hyaluronidase is characterized, in the normal subject, by a series of modifications of the resorption-image (figs. 1A and 1B). Under the influence of the enzyme, on the one hand, a more rapid and clearly defined formation of the reticular pattern with greater distinct limits is obtained and, on the other hand, the disappearance of the contrast substance is markedly accelerated.

This action of the hyaluronidase may be explained by an increase of permeability of the ground substance of the tissues, which results in an easier diffusion of the contrast substance and in its accelerated resorption following a more outspread and more rapid contact with the capillary system.

In a previous work (1955), we studied the microradiographies of the inner wall of Schlemm's canal after injection of Thorotrast into the anterior chamber of the human enucleated eye.

We have been able to demonstrate a direct communication between the anterior chamber and Schlemm's canal and, inside the scleral trabecula, a system of clefts emptying directly through orifices into Schlemm's canal.

Injecting into the anterior chamber suspensions of Angiopac with particles of a

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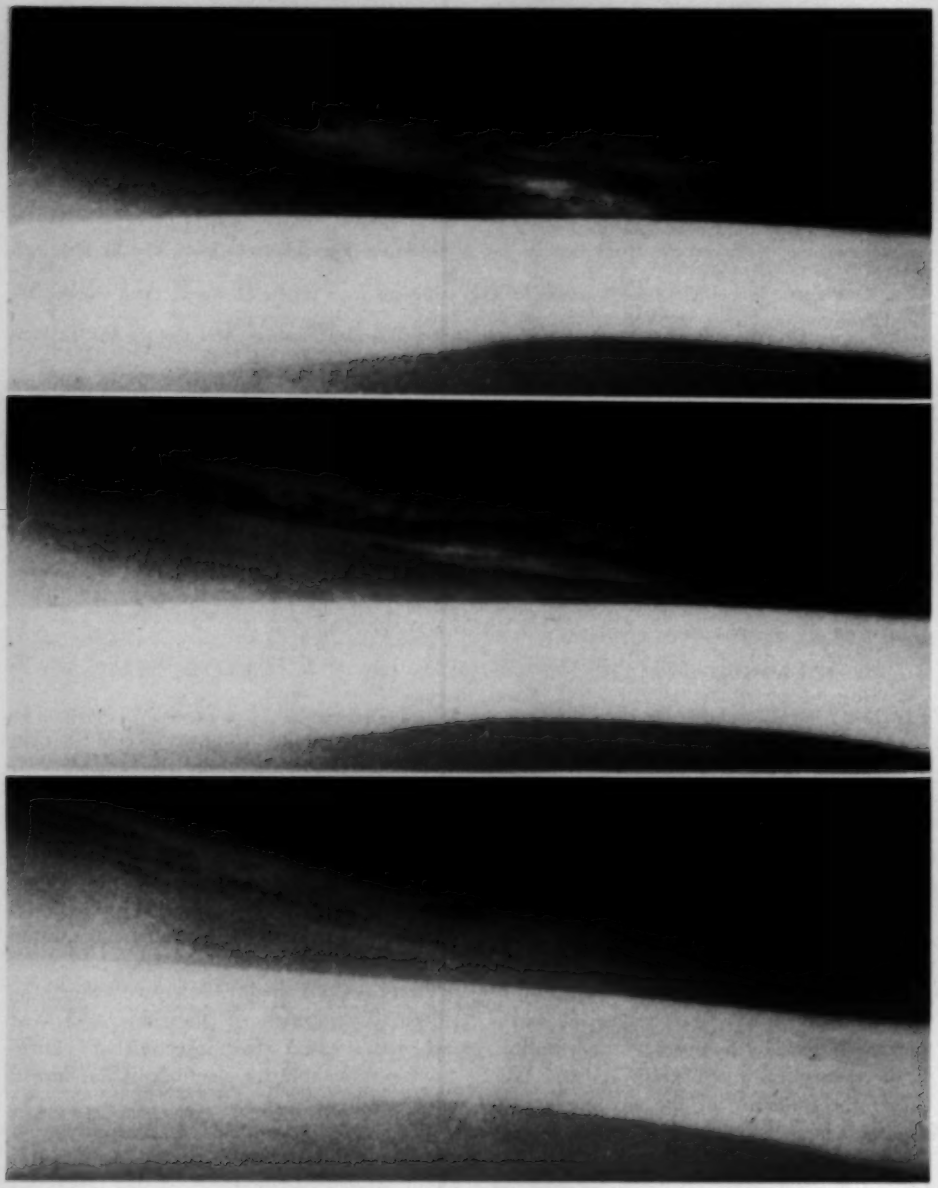

Fig. 1A (François, Neetens, and Collette). Normal image. Normal subject. Action of hyaluronidase on the resorption picture after subcutaneous injection of a contrast substance (Umbradil). (Top) Zero minutes; (center) after 15 minutes; (bottom) after 60 minutes.

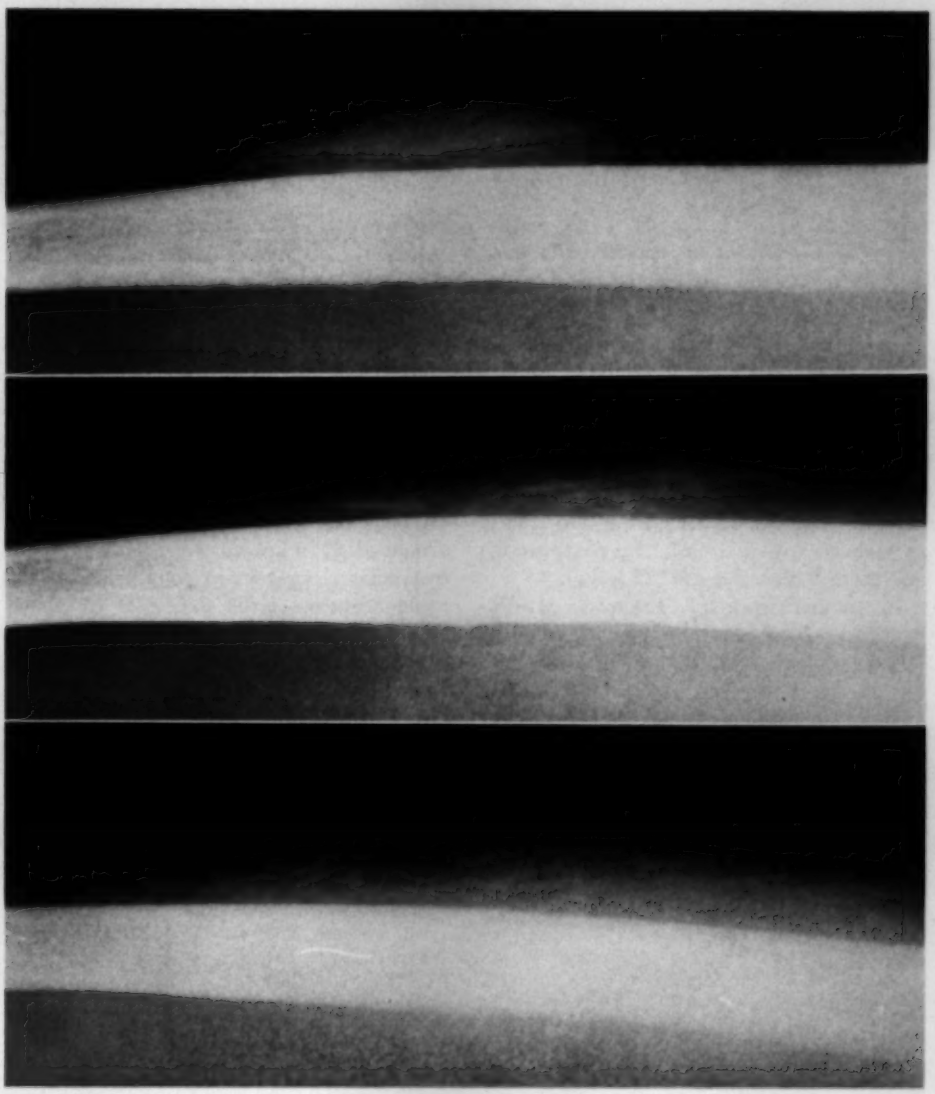

Fig. 1B (François, Neetens, and Collette). Acceleration of the collector phase, better outlined reticulum, accelerated resorption. Normal subject. (Top) Zero minutes; (center) after 15 minutes; (bottom) after 60 minutes.

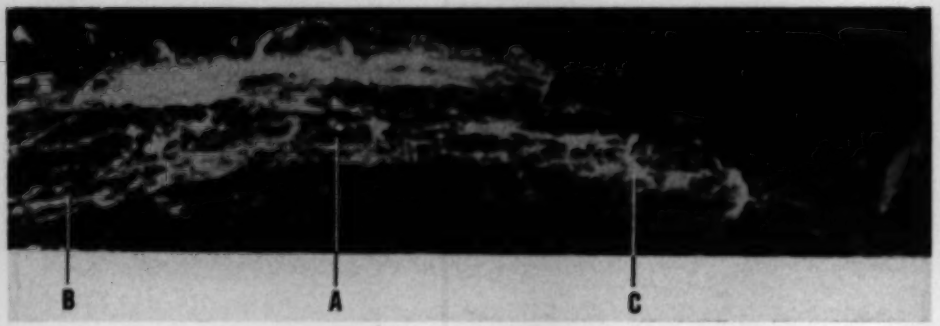

Fig. 2 (François, Neetens, and Collette). Inner wall of Schlemm's canal after treatment with hyaluronidase and injection of Thorotrast into the anterior chamber. (A) Reticular pattern with distinctly outlined limits. (B) Circular stripes have a tendency to lengthen. (C) Fewer white spots; canalicular radiating stripes, which are slightly tortuous with sharp contrast, appear. (Or., ×80.)

constant size for a determinate sample, we could demonstrate that the width of the orifices measures between 1.5 μ and 2.25 μ, as particles with a size of 1.5 μ pass through and those with a size of 2.25 μ do not.

In another work (J. François, M. Rabaey, and A. Neetens, 1955), suggested by Bárány's researches (1954), we have demonstrated that in the human enucleated eye, after perfusion of the anterior chamber with hyaluronidase, the facility of outflow (C) increases with an average value of 25 to 30 percent.

Under these conditions we wonder on which anatomic, physiologic, and biochemical facts the action of the hyaluronidase is grounded. It is known that the walls of the trabecular clefts contain polymerized hyaluronic acid, the large molecules of which, according to a hypothesis of Bárány, may block small pores. So it is possible that the hyaluronidase, breaking the hyaluronic acid down and altering the ground substance, not only opens new orifices but also widens the trabecular clefts already present.

The present microradiographic study of

Fig. 3 (François, Neetens, and Collette). Inner wall of Schlemm's canal after treatment with hyaluronidase. Injection of Thorotrast into the anterior chamber. (X) Hazy appearance between the reticular pattern. (Or., ×120.)

the inner wall of Schlemm's canal constitutes a contribution to the solution of this problem. The experimental and radiologic techniques are identical to those used in our first study, with the only difference that the Angiopac and Thorotrast have been perfused under a physiologic pressure of 20 mm. Hg, and after previous injection of hyaluronidase under the same pressure into the anterior chamber.

Results

1. If there is an increase in diameter of the orifices of the inner wall of Schlemm's canal, this must be very small. The maximal diameter does not exceed 2.25 μ, as an Angiopac suspension with particles measuring 2.25 μ does not penetrate into the canal.

2. The microradiographies, after injection of Thorotrast into the anterior chamber, following treatment with hyaluronidase (figs. 2, 3, 4, and 6), show an image different from that obtained without previous treatment with the enzyme (fig. 5).

a. The irregular and hazy patterns, not very dense or opaque, with mostly longitudinal or circular direction, are not wholly found again. We observe on the contrary a much more outlined reticular image with more distinct limits, the circular stripes having a tendency to lengthen and to continue in a more or less uninterrupted manner (figs. 2 and 4).

b. If the hazy appearance (penumbra) of certain clefts has disappeared, the trabecular lamellae themselves, which did not contain previously a single trace of Thorotrast, appear actually infiltrated by contrast substance: this observation may indicate that the tissue itself has become more permeable (figs. 3 and 6).

c. The white spots more or less round or

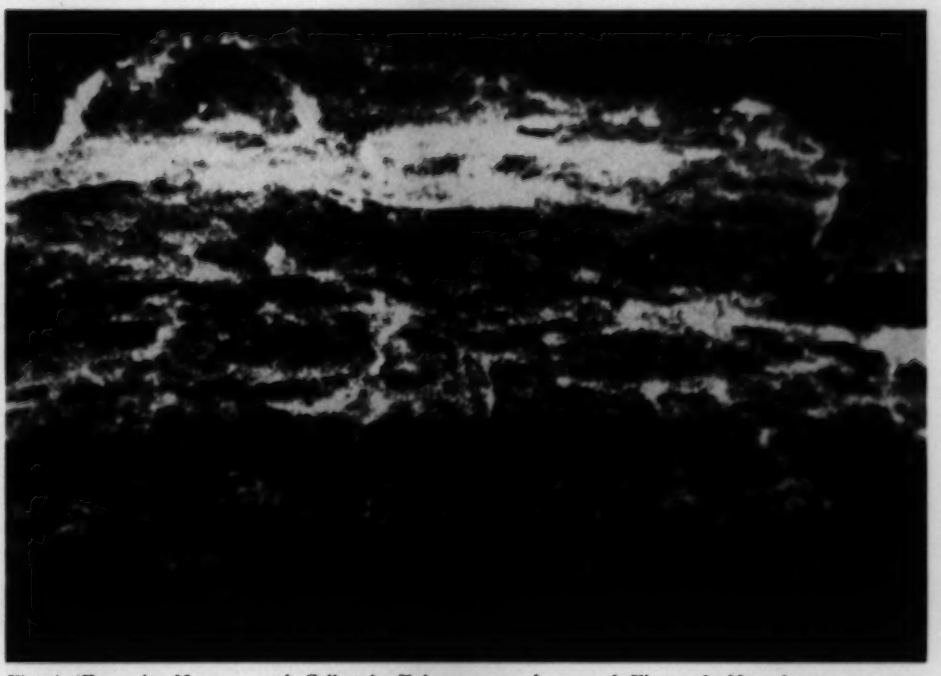

Fig. 4 (François, Neetens, and Collette). Enlargement of part of Figure 2. Note hazy appearance between the cleft images. (Or., ×195.)

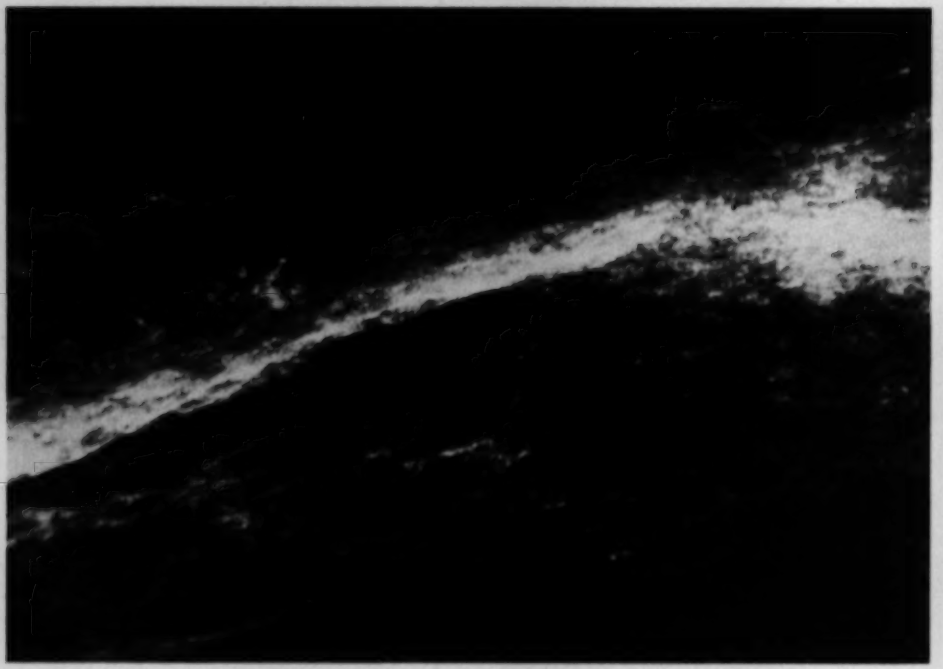

Fig. 5 (François, Neetens, and Collette). Posterior inner wall of Schlemm's canal, without previous treatment with hyaluronidase. Injection of Thorotrast into the anterior chamber. (Or., ×195.)

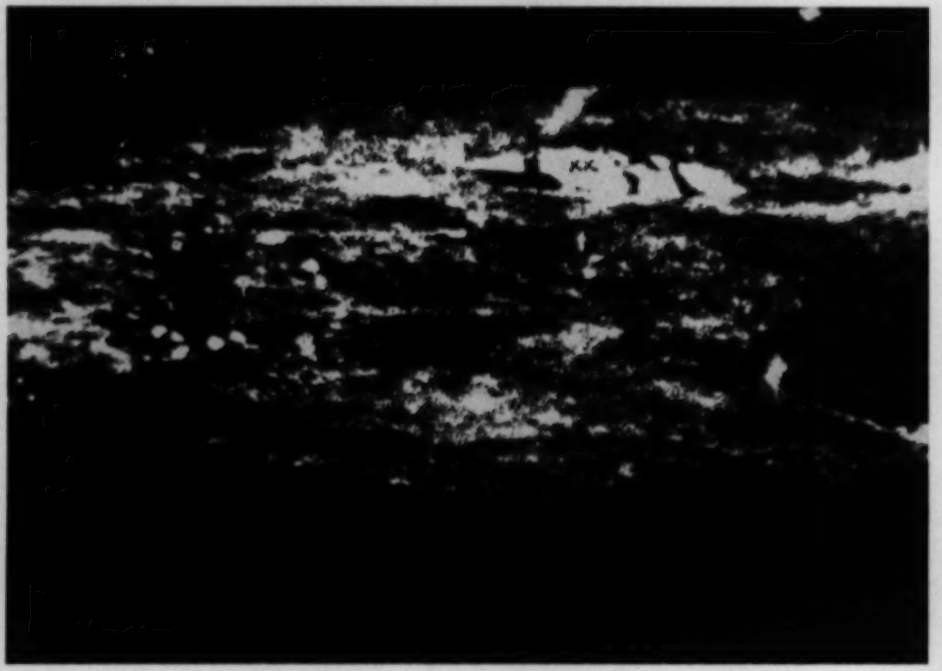

Fig. 6 (François, Neetens, and Collette). Posterior inner wall of Schlemm's canal after treatment with hyaluronidase. Injection of Thorotrast into anterior chamber. (XX) Artefact. Note how the hazy appearance (X) of the tissue itself differs from that shown in Figure 5. (Or., ×195.)

oval and also the fine very opaque radiate stripes, in relation to these spots, have diminished in number.

d. Circular patterns no longer predominate, but radiate patterns frequently occur; indeed, radiate canalicular and slightly tortuous stripes appear. They are strongly white because of the very heavy contrast-intensity (fig. 2).

We may wonder if these stripes are collector channels of enlarged clefts that debouch into the orifices previously described (white spots), or if they represent a change in the direction of the trabecular clefts following a structural modification. The first hypothesis seems to us to be the more plausible.

Conclusions

From our observations, we may conclude:

1. That the trabecular clefts and their orifices at the level of the inner wall of Schlemm's canal are enlarged but only in a very poor manner.

2. That the permeability of the connective tissue, building up the trabeculae, has increased.

3. That there is no evidence that new orifices are added to those already existing, but that the passage of the contrast fluid occurs in a more direct manner.

2, Avenue Pasteur.

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CORRECTION OF SPASTIC ENTROPION*

By the method proposed by Wies

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The treatment of spastic or senile entropion, though occupying a small place in the field of ophthalmology and ophthalmic surgery, is nevertheless a perplexing, and often disappointing, challenge to the ophthalmologist. The procedure for correction of spastic entropion which is here reported, though not widely known, was first described in the fall of 1953 and later published in June, 1954.[1] On the basis of the excellent results reported, and in view of the fact that previous methods for the correction of spastic entropion have too often been disappointing, an endeavor has been made to collect a series of cases over the past 16 months which were operated by the method proposed by Dr. F. A. Wies.

Though many factors are involved in the production of senile or spastic entropion, it is reasonable to conclude as Kettesy[2] pointed

* From the Manhattan Eye, Ear, and Throat Hospital. Presented before the New York Academy of Ophthalmology, Section of Ophthalmology, March, 1955.

out in 1948 that the prime factor is a drawing up and accumulation of bundles of the palpebral portion of the orbicularis muscle in the lid margin, secondary to a slackening and atrophy of the palpebral connective tissue. The entropion occurs on contraction of the muscle and is not likely to be self-reducing, since the corneal irritation so produced often sets up a secondary spasm which may be severe.

Duke-Elder[3] points out that the palpebral orbicularis forms two arcs as it lies in its normal anatomic relationship against the lower tarsal plate. The concavity of one arc is directed posteriorly, that of the other superiorly. Contraction of the muscle, therefore, has the effect of reducing these two arcs to chords and, in the absence of normal connective tissue support, the muscle bundles accumulate in the lid margin and have a posterior direction of force.

Operations for the correction of spastic entropion should, therefore, be directed toward preventing this upward riding of the muscle bundles over the tarsus. This can be accomplished in one of several ways:

First, by re-establishing the absent pressure of the muscle on the convexity of the lower tarsal plate, as exemplified by the Wheeler technique.

Second, by producing fibrous tissue adhesions between the muscle and the tarsal plate, which is the primary purpose of the Ziegler cautery and a secondary effect of practically all of the many methods which employ a surgical incision through the muscle.

Third, by producing an actual tissue barrier which divides the muscle, and, therefore, will not permit migration of its lower fibers into the lid margin. This is the purpose of the Wies procedure.

Other principles have been proposed, such as increasing the tone of the tarso-orbital fascia and even complete excision of the palpebral and part of the orbital portions of the orbicularis. These procedures do not, however, attack the problem directly or, as in the latter technique, are more severe than is generally warranted.

	SATISFACTORY	UNSATISFACTORY
WHEELER (27 CASES)	56 %	44 %
ZIEGLER (15 CASES)	47 %	53 %
WIES (18 CASES)	78 %	22 %

Fig. 1 (McFarlane). Postoperative results in 60 cases of spastic entropion.

In order to compare the results using the Wies method, all of the cases of spastic entropion operated on the clinical service of the Manhattan Eye, Ear, and Throat Hospital over the past five years have been reviewed. Only those cases in which the follow-up was six months or more have been recorded for comparative purposes. None of the Wies-procedure cases reported is less than three months postoperative.

This series (fig. 1) shows less than a 60 percent cure rate when the Wheeler method was used and less than 50 percent when Ziegler cautery was employed as compared to better than 75-percent cure with the Wies procedure. The relatively small number of Ziegler cauterizations is due to the fact that only those performed in the operating room are included. Undoubtedly results of many of the less severe cases treated by cauterization in the out-patient clinic would change this figure. I have not included procedures other than those mentioned, since only a small number of cases representing each of numerous and varied other methods of treatment could be collected.

	SATISFACTORY		UNSATISFACTORY		
	GOOD FUNCTIONAL AND COSMETIC RESULT	GOOD FUNCTIONAL RESULT	RECURRENCE	OVERCORRECTION MILD	OVERCORRECTION SEVERE
WHEELER	14	1	11	1	0
ZIEGLER	5	2	7	1	0
WIES	11	3	0	1	3

Fig. 2 (McFarlane). Postoperative analysis of 60 cases of spastic entropion.

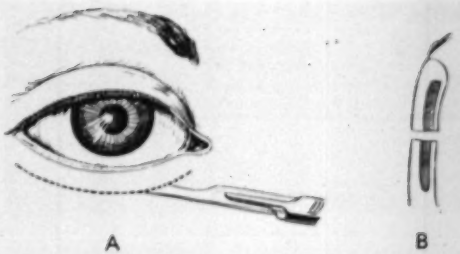

Fig. 3 (McFarlane). (A) Conjunctival incision made the length of the lower lid. No fixation clamp or ocular protector is shown. (B) Cross section of lid following incision no more than four mm. below the lid margin. Artist's conception of tarsus below incision is exaggerated.

A more detailed analysis of the cases (fig. 2) demonstrates one point clearly. Cases treated by both the Wheeler and Zielger methods show a marked tendency to recurrence, even after several months, while those treated by the Wies method do not. The Wies method, on the other hand, shows a tendency toward overcorrection in an unselected series, a difficulty which I feel can be largely eliminated by attention to the technique.

Method of operation

The technique recommended by Dr. Wies, and the one which has been followed, can be done as an office procedure if adequate assistance is available.

Under local infiltration anesthesia, a horizontal through-and-through incision, to include skin, muscle, tarsus, and conjunctiva, is made the length of the lower lid and four mm. below its margin (fig. 3). Hemostasis is readily achieved by pressure. Three 4-0 black silk, double-armed sutures are placed in the free margin of the conjunctiva (fig. 4) at the lower edge of the incision and brought out through the skin of the upper part, where they are tied over rubber pegs or a continuous rubber strip. The skin edges are then closed with interrupted 6-0 silk sutures. This effectively incarcerates a tongue of conjunctiva within the wound and above the major portion of the lower palpebral orbicularis fibers.

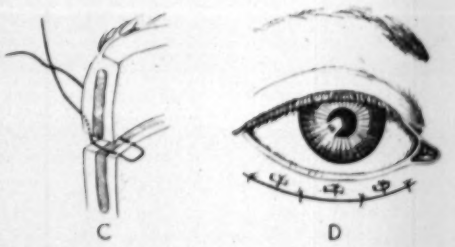

Fig. 4 (McFarlane). (C) Showing double-armed, 4-0 black-silk suture passed through conjunctiva of the lower part of incision and emerging through skin of the upper part. (D) Deep sutures in position and secured over rubber pegs. Skin closure with interrupted 6-0 silk.

Experience has taught that the most important part of the procedure is the lid incision. This should be made perpendicular to the lid and no more than four mm. below its margin, after first outlining the incision with marking fluid. If local anesthesia is used, it is best to block the lid rather than infiltrate directly into the area of the incision. To facilitate an incision perpendicular to the surface of the lid, a fixation device, such as the Erhardt clamp, is extremely helpful. Practically all of the overcorrections encountered have been attributed to an incision which is either too far below the lid margin, or is slanted downward and posteriorly into the lower fornix.

It has not been found necessary to undermine the conjunctiva which is to be incarcerated in the wound. The deep sutures are usually removed on the third or fourth day and the skin sutures on the fifth or sixth. Several of our successful cases have shown an apparent early overcorrection which persists as long as two or even three weeks. The overcorrections regress, however, without treatment or, if pronounced, it may be advisable to remove the offending deep suture or sutures at the first dressing. In the event that overcorrection occurs, application of the cautery to the conjunctival surface of the lid, as recommended by Wies, should be sufficient to control the ectropion.

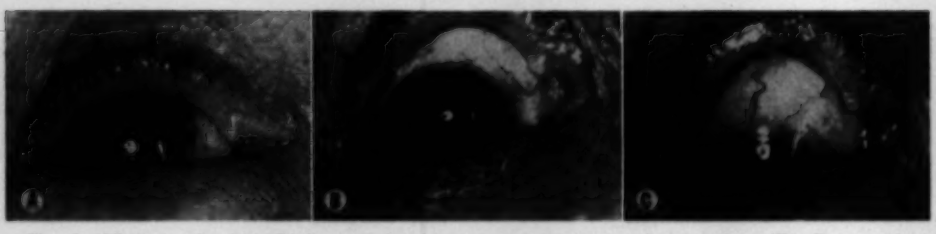

Fig. 5 (McFarlane). (A) Right eye, showing severe constant spastic entropion. (B) Same patient, nine weeks postoperative, showing lower lid in good position. Upper lid, manually retracted. (C) Nine weeks after operation, showing attempt to produce inversion of lower lid by forced closure, while upper lid is held in position.

Summary

A little known method for the correction of spastic entropion, based on attacking what is believed to be the primary etiologic factors of this condition, has been presented. Results from this operation are gratifying (fig. 5-A, B, and C). Though there is a tendency to overcorrection in an unselected series, proper attention to the details of the procedure, especially as regards the lid incision, should overcome this fault. No recurrences are reported, despite the fact that many of the procedures were performed on persons with a history of as many as three previous operations for spastic entropion on the same lid. The procedure seems to be an operation of choice in severe and recurrent spastic entropion.

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IDIOPATHIC RETINAL DETACHMENT*

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In normal eyes the vitreous adheres to the region of the optic nerve and—more firmly—to the periphery. In other parts of the adult human retina, however, no adhesions between retina and vitreous are generally supposed to exist.

In cases of retinal detachment, nevertheless, tiny strands may be seen with the ophthalmoscope which are apparently pulling small flaps, even small isolated pieces of the ruptured retina, into the vitreous space. They have been described in pathologic specimens as the result of a degenerative or postinflammatory condition of the vitreous body and retina.

In some publications, the suggestion may be found that alterations in the retina and vitreous body might secondarily enforce preexistent tiny adhesions to firmer connections, which have a pathogenetic significance in the development of retinal tears (Hruby[1]). However, as far as we know, no histologic evidence was given to substantiate these theories.

In 1952, one of us (Hagedoorn) demon-

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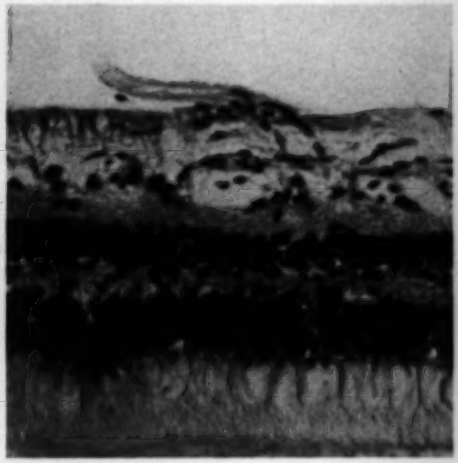

Fig. 1 (Hagedoorn and Sieger). The strand emerging from the retina and entering the vitreous space has a delicate fibrous structure in its intravitreal course.

strated some sections, showing apparent congenital adhesions between retina and vitreous body. (Sheffield lecture, 1952.) The eye was enucleated in a child, aged nine months, with a diagnosis of pseudoglioma, a diagnosis which could not be confirmed by the microscopic examination. A pit in the optic nerve

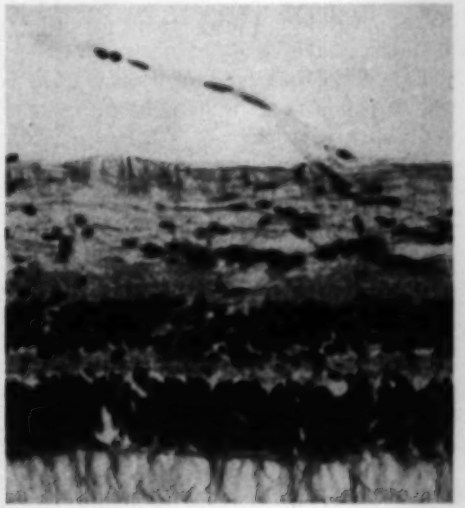

Fig. 2 (Hagedoorn and Sieger). A similar but more delicate strand penetrates into the vitreous.

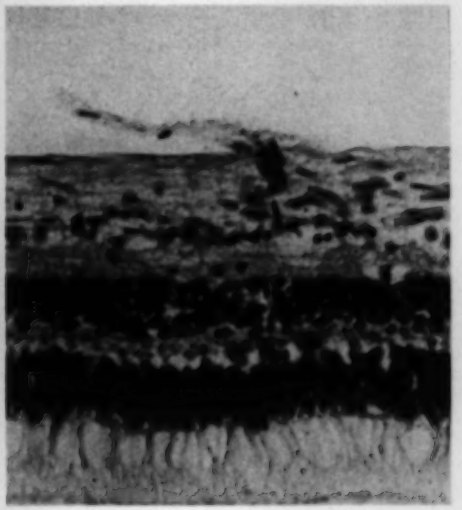

Fig. 3 (Hagedoorn and Sieger). The cells at the base of the strand are more numerous and well stained.

was found and had been described in 1928 (Hagedoorn[2]). The adhesions between retina and vitreous body will now be described in greater detail:

Figures 1, 2, and 3 show strands emerging from the retina and entering the vitreous space. These were situated in the equatorial region of the retina.

In Figure 1, the strand has a delicate fibrous structure in its intravitreal course. It is only just after emergence from the retina that a number of cells of varying shapes can be seen. The course of this strand, curving to a more perpendicular position upon entering the retina, is apparently indicated further on in the retinal tissue by the position of some oblong nuclei, lying with their long axes parallel to the Müllerian fibers. One small, intensively staining, nucleus is seen between the strand and the retina.

In Figure 2, a similar but more delicate, strand penetrates into the vitreous, containing three oblong, pale nuclei and two small dark nuclei at the end. A similar, small dark nucleus is seen to lie free on the retina and another close to the strand.

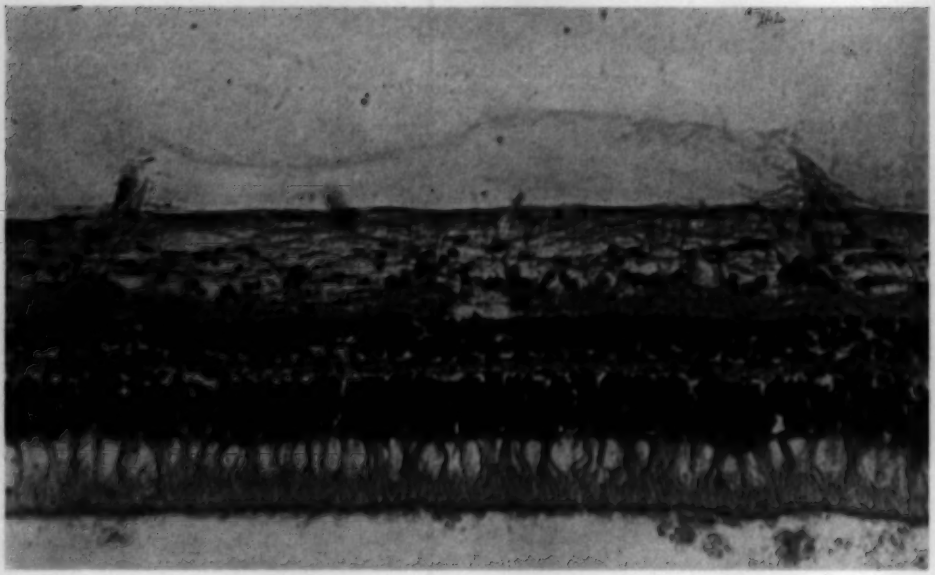

Fig. 4 (Hagedoorn and Sieger). Another variety of retinal-vitreous adhesion.

A nearly identical picture is seen in Figure 3 where the cells at the base of the strand are more numerous and well stained. These are mostly oblong and their long axes are perpendicular to the surface of the retina. An isolated oblong nucleus in the same perpendicular position is seen halfway between the inner nuclear layer and the surface of the retina. Two pale nuclei may be traced in the intravitreous part of the strand.

In Figure 4, another variety of retinal-vitreous adhesion is seen. It is shorter, more loosely fibrillar, emerging through the inner surface of the retina over a relatively large area compared with its intravitreal extension. The emerging, tiny fibers converge in their intravitreal course, so that a delicate pyramid of fibrillar tissue is seen on the inner surface of the retina. Several fibers may be traced into the retinal tissue. Only a few nuclei or fragments of nuclei are seen in these little pyramids. A structureless strand of condensed vitreous tissue is attached to the top of the pyramids, and it might be suggested that fibrils of the pyramids appear to fade into this strand.

In Figure 5, the fibers of three more delicate fibrous pyramids may be traced through the internal limiting membrane into the retinal tissue.

In Figure 6, the adhesion has a more diffuse character. A tiny strand parallel to the retina contains one dark nucleus; another nucleus is seen on the retinal surface and a globule with several nuclei is floating freely in the vitreous space.

These anomalies have certain features in common:

1. There is no relation with vessels or vessel sheaths.

2. They have a fibrillar character and the intraretinal course of the fibers is parallel to the course of the Müllerian fibers.

3. They are associated with nuclei, which at least partly suggest the presence of viable elements on the surface of the retina, capable of fibrogenetic activity.

4. In studying these sections there is hardly any doubt possible as to the ectodermal nature of these anomalies.

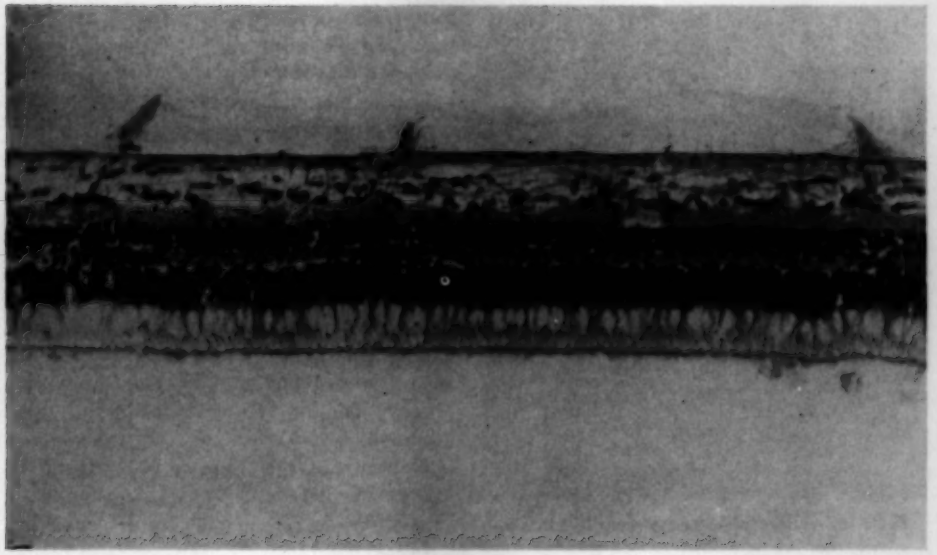

Fig. 5 (Hagedoorn and Sieger). Fibers of three more delicate fibrous pyramids may be traced through the internal limiting membrane into the retinal tissue.

5. The gradual fading away or transition into vitreous tissue supports the view that they are related in some stage of the embryonic development to the vitreous body and its formation. Normal regression has failed to occur; they have persisted and developed further as a consequence of the growth of the whole organism.

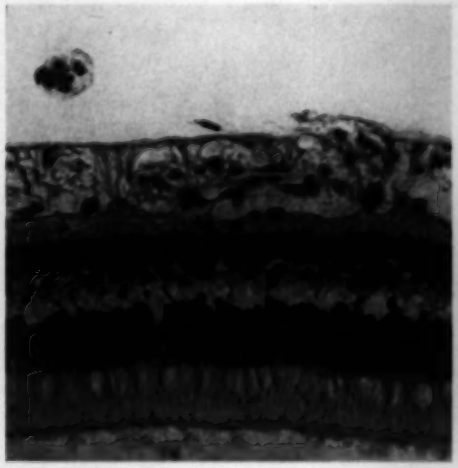

Fig. 6 (Hagedoorn and Sieger). This adhesion has a more diffuse character.

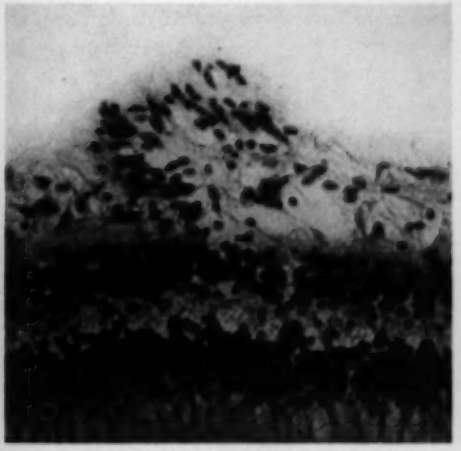

Fig. 7 (Hagedoorn and Sieger). A proliferation of retinal cells and tissue from the superficial layer of the retina.

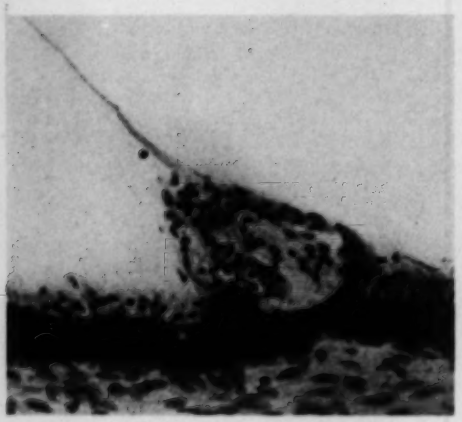

Fig. 8 (Hagedoorn and Sieger). Tissue proliferation in the region of the pars plana resulted in a peculiar pear-shaped formation.

Further evidence of the ectodermal nature of the anomalies may be seen in unusual findings of a somewhat different nature:

Figure 7 pictures a proliferation of retinal cells and tissue from the superficial layer of the retina. It is hazardous to try to identify these cells, but they resemble the cells seen in the base of the vitreoretinal adhesion of Figure 3 and the globule in the vitreous of Figure 6. Partly by their aspect, partly by comparison it seems reasonable to conclude that they are related to the ectodermal supporting tissue of the retina.

Conclusive evidence regarding the nature of the anomalies described was found in the more important anomalies in the pars plana of the retina:

In Figure 8 a tissue proliferation in the region of the pars plana resulted in a peculiar pear-shaped formation ending in a thick "zonular fiber."

A similar formation is presented in Figure 9. The loose tissue is indicative of a relation with the vitreous and zonula. A typical "rosette" indicates the relationship to retinoblasts.

In Figure 10 the tendency to proliferation of the retinal cells is restricted to the basal region, where large oblong nuclei are seen, whereas the pyramid consists of acellular "zonular" material only.

From these latter anomalies, which were found in various regions of the retina, it is clear that equilibrium in the share of ectoderm and mesoderm in the formation of the vitreous has been disturbed in a very early stage of development. The temporary task of the ectoderm in its formation ends at a very early stage under normal conditions.

Fig. 9 (Hagedoorn and Sieger). A formation similar to that shown in Figure 8.

Regression has evidently been delayed; even a limited outgrowth, though local and irregular, followed.

Since, as far as we know, similar congenital retinovitreal adhesions have not been described in literature, we may have come upon an extremely rare specimen with a very limited value in relation to the strands often associated with tears in the retina. Consequently, we studied sections in an effort to trace such adhesions in normal eyes.

We finally succeeded in finding a retinovitreal strand, evidently of the same nature as the strands found in the eye with the congenital anomalies. The adhesion is delicate, but an identical arrangement of cells at the point of emergence in the retina seems to be conclusive evidence (fig. 11). The eye was enucleated post mortem in a man who died at the Department of Internal Diseases with a diagnosis of sprue. With the exception of a few tiny hemorrhages in the retina the eye was completely normal in all other respects.

Consequently, we felt justified in concluding that in some cases of retinal detachment congenital "microanomalies" may be responsible for the pathogenesis of retinal tears.

Fig. 11 (Hagedoorn and Sieger). An adhesion discovered in an otherwise normal eye.

Fig. 10 (Hagedoorn and Sieger). The tendency to proliferation of the retinal cells is restricted to the basal region.

One of us (Sieger) came upon a clinical case in which such a pathogenesis seems probable:

A man, aged 60 years, complained of the sudden appearance of spots in front of the right eye. There was one diopter of hypermetropia and normal vision in both eyes. The nature of the subjective symptoms suggested the presence of a posterior detachment of the vitreous body.

On ophthalmoscopic examination, the diagnosis was confirmed and the typical ring-shaped opacity was seen to float in the vitreous anterior to the optic disc. In examining the fundus of both eyes no other anomalies, cicatrices, pigmentations, or degeneration could be traced. There were no senile degenerations, the fundi could be considered to be completely normal.

At the equatorial region at the temporal side of the right eye, however, a hole was seen in the retina. It was small and round, with an operculum in front of it, surrounded by tiny hemorrhages, similar to those described by de Vries[3] in some cases of detach-

Fig. 12 (Hagedoorn and Sieger). From a colored drawing. At the equatorial region at the temporal side of the right eye, a hole was seen in the retina. Otherwise, the eye was apparently normal.

ment of the vitreous body around the optic nerve. We carefully examined the region of the hole and could not find any trace of preceding inflammation or degeneration. It had to be concluded that a piece of retina had been torn out by some mysterious force (fig. 12).

It seems reasonable to identify this mysterious force with the pull at a congenital vitreoretinal adhesion of the type described in the preceding pages. The detachment of the vitreous from its insertion around the disc allowed a retraction of the vitreous and consequently a considerable pull on the vitreoretinal adhesion.

Finally, we found a case in which a piece of retina was torn out. We had been searching for such a case for a long time and, although several cases were found in which this pathogenesis seemed possible, in none was there such complete evidence of the development of a rupture in an otherwise completely normal eye.

It might be argued that a constant pull at these adhesions might give rise to some secondary alterations in the adjacent retina or underlying choroid suggesting inflammatory or degenerative changes (Schepens[4]). However attractive these speculations may be, only in our case was there substantial evidence—as far as is possible by ophthalmic examination—that congenital adhesions might cause retinal ruptures in otherwise completely normal eyes.

From the length of time which has elapsed since we focussed special attention on this subject (from 1952) before finding this case, it may be concluded that they are of rare occurrence in their "pure form." Moreover, from a mechanical standpoint a detachment of the vitreous would have to be considered a precursor of a retinal tear and of the subsequent development of a detachment. It is clinical experience, however, that a detachment of the vitreous body is rarely followed by a detachment of the retina. It will be remembered that Gonin stressed the importance of traction from the vitreous in the pathogenesis of retinal detachment.

Favre[5] examined the anterosuperior insertion of the vitreous in cases of total vitreous detachment, with the aid of a contact lens with three mirrors. He describes a distinct form, the perpendicular insertion, which causes a maximum of traction. This form occurs in 25 percent of the cases of total vitreous detachment.

Consequently, cases of what may be called "idiopathic detachment of the retina" may be relatively rare.

This, however, does not exclude that vitreoretinal adhesions of the congenital type are playing a role in other cases of retinal detachment. It seems reasonable to accept the possibility that they may be less pronounced but, nevertheless, in combination with later degenerative or inflammatory processes, may constitute the basis or framework on which firmer degenerative vitreoretinal adhesions develop.

Such varieties of adhesions as are pictured in Figure 4 and Figure 5 lend special sup-

port to this theory. Here a typical homogenous condensation in the vitreous is adherent to the little fibrillar pyramid in the retina. Moreover, retinal cells are, possibly, associated with formation of "vitreoid" material outside the retina. Nothing can be said as to their viability and activity in abnormal circumstances and their eventual share in the development of the strong vitreoretinal adhesions associated with ruptures in cases of retinal detachment.

Summary

Congenital retinovitreal adhesions may play a role in the pathogenesis of retinal detachment; they may explain cases of "idiopathic" detachment; they may be involved in the pathogenetic process resulting in the formation of strands associated with the formation of flaps and opercula in other cases of retinal detachment.

Wilhelmina-Gasthuis.

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EXPERIMENTAL STUDIES WITH ACETAZOLEAMIDE IN ANAPHYLACTIC IRIDOCYCLITIS IN RABBITS*

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During the past two years, acetazoleamide (Diamox) has been generally used to decrease intraocular pressure in glaucoma. There are a few reports in the literature on the action of this drug in secondary glaucoma. Becker[1] observed a lowering of increased intraocular pressure in secondary glaucoma in a number of patients. Breinin and Görtz[2] studied a patient with secondary glaucoma in whom a high intraocular pressure returned to normal on acetazoleamide, and the inflammatory process was later readily controled by atropine and cortisone. Grant and Trotter[3] observed a lowering of pressure in two cases of acute secondary glaucoma with Diamox when standard local treatment was inadequate. The iridocyclitis subsided in both cases during treatment with this drug. In a small series of patients with secondary glaucoma at the Toronto General Hospital, acetazoleamide brought about a rapid reduction in intraocular pressure and an apparent improvement in the inflammatory condition.

Experiments with rabbits have been carried out to determine the effect of acetazoleamide on eyes with intraocular inflammation and secondary increase in intraocular pressure.

Methods and Materials

Allergic iridocyclitis was induced in the eyes of dark-pigmented rabbits by the intravitreal injection of 0.07 cc. of horse serum. This method resulted in a less violent reaction than that in which the rabbit was previously sensitized by a parenteral injection of the protein. A slight aqueous flare was

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seen for about two days following the intravitreal injection and then disappeared. After an interval of seven to 10 days, the flare reappeared, increased over a period of several days, and then remained constant for about 10 days. It disappeared from 18 to 23 days after onset. The constant period was used for the testing of acetazoleamide.

The following estimations were undertaken:

1. *Fluorescein estimations* were taken immediately after the intravenous injection of 0.01 cc. of a stock solution of 10-percent fluorescein, and at 10-minute intervals thereafter. The apparatus described by Hodgson and MacDonald[4] was used to determine the minimal slitlamp illumination necessary for the recognition of threshold-green. Ampere readings were converted into approximate fluorescein concentrations per hundred million.

2. *Aqueous flare* was determined by tyndallometry, in which the concentration of colloidal particles was inversely proportional to the strength of the examining beam. Since the same principle was involved as in the measurement of fluorescein concentration, the same apparatus was applicable to these determinations. The threshold appearance of the flare indicated the aqueous protein concentration. Values obtained were arbitrary numbers, and did not bear a simple relationship to the actual protein concentration. Nevertheless they could be used as a very sensitive test of the relative increase or decrease of aqueous protein concentration.

3. *Tonometry* was carried out with a Schiøtz tonometer.

Procedure

1. Determination of the masking effect of protein upon fluorescein

In order to determine whether colloidal particles in the aqueous would cause masking of fluorescein, the following experiment was carried out:

A stock solution of fluorescein, diluted to a concentration of five parts in 100,000,000, placed in a Beckman cuvette with a fresh rabbit cornea between it and the slitlamp, gave a reading of 3.5 amperes. This fluorescein dilution was then mixed with increasing proportions of re-calcified plasma. The lowest concentration of plasma which gave masking of the dye was 10 percent. All animals with a tyndallometric reading below 3.2 amperes indicating protein concentration in excess of 10 percent were not used where the fluorescein method was concerned.

2. Determination of the effect of diuresis due to acetazoleamide on the fluorescein excretion by the kidney, and on ocular tension

Since acetazoleamide causes a diuresis through the kidney, it was necessary to determine if the increased flow of urine resulted in an increased excretion of fluorescein, since this would affect all fluorescein concentrations in the aqueous. Similarly, it was of interest to see if this diuresis would effect intraocular pressure.

Five rabbits with secondary glaucoma were placed separately in stainless steel boxes. The urine excretion and its fluorescein concentration were measured every two hours. Ocular tension was also recorded at two-hour intervals. After establishing the base-line, six mg. of acetazoleamide per kg. of body weight were given by the intravenous route to each rabbit. There was a rapid fall in the ocular tension with the lowest reading recorded within the first two hours. Diuresis was insignificantly increased in two hours, and could not have been responsible for the fall in tension. On continuous dosage of the drug, urinary excretion became constant and remained above normal after 48 hours. Fluorescein concentrations in the urine were found to be inversely proportional to volume. The dye thus acted as a low threshold substance, and its urinary excretion seemed to be independent of diuresis.

3. The effect of acetazoleamide

As a result of the study of 37 rabbits with primary anaphylactic iridocyclitis treated

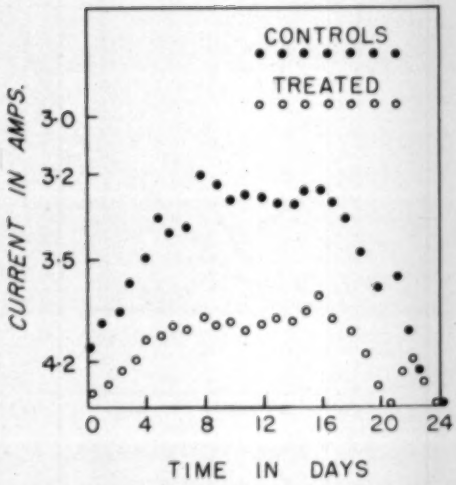

Fig. 1 (Schirmer and Ormsby). *Tyndallometry.* The effect of acetazoleamide on aqueous protein flare (Group A). Average values.

with acetazoleamide, it was found that they comprised three groups: Group A, 17 without tension increase; Group B, 12 with tension increase which was reduced to normal with acetazoleamide; and Group C, eight with tension increase which responded poorly to the drug.

Group A. The aqueous protein flare in 10 rabbits treated throughout the course of their reaction with acetazoleamide (30 mg. per kg. of body weight per day was compared with that of 10 control rabbits with iridocyclitis which received no treatment (fig. 1). It will be seen that the flare was less intense in the treated than in the untreated animals. Upon disappearance of the flare on about the 21st day in the treated rabbits, the drug was discontinued, whereupon the flare reappeared, and from that time on, paralleled that of the controls.

Another group of rabbits with iridocyclitis, without increase of tension, were treated with the same dosage of acetazoleamide for two days after the onset of the reaction. Upon cessation of treatment (fig. 2), there was a rapid increase in aqueous flare measured by tyndallometry. These animals were also studied by the fluorescein method, and

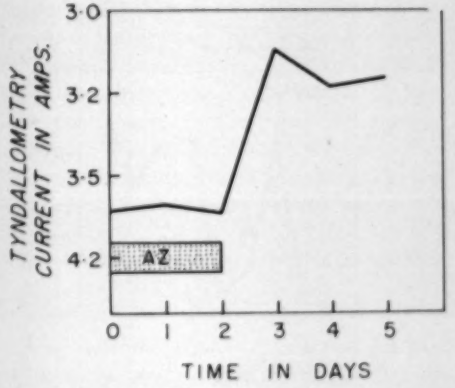

Fig. 2 (Schirmer and Ormsby). *Tyndallometry.* The effect of discontinuing acetazoleamide on aqueous flare (Group A). Average values.

the fluorescein concentration in the aqueous during treatment was lower than it was in the same animals after treatment was discontinued (fig. 3). This decrease in fluorescein concentration in the aqueous under acetazoleamide appeared to be quantitatively less significant than the decrease in protein flare as measured by tyndallometry.

Group B. In animals in Group B, the withdrawal of continuous dosage of acetazoleamide was followed by a rapid increase in

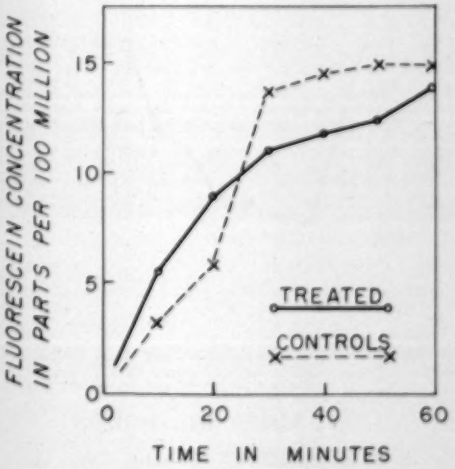

Fig. 3 (Schirmer and Ormsby). *Fluorescein test* before and after treatment (Group A). Average values.

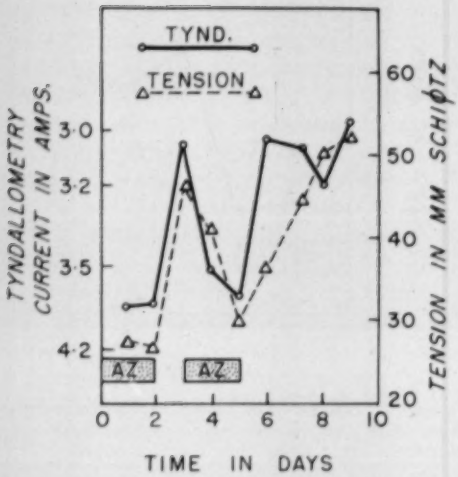

Fig. 4 (Schirmer and Ormsby). Effect of acetazoleamide on intraocular pressure and protein flare (Group B). Average values.

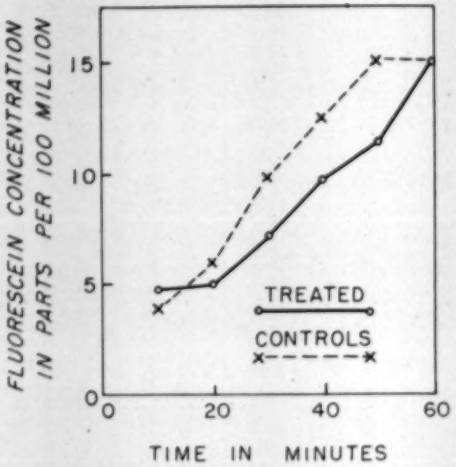

Fig. 6 (Schirmer and Ormsby). *Fluorescein test* before and after acetazoleamide (Group B). Average values.

intraocular pressure and this was paralleled by an increase in aqueous protein flare (fig. 4). Upon further treatment, the flare and tension were again promptly reduced. Following a single intravenous injection of the drug in animals in this group (fig. 5), there was a rapid decrease in tension which was maintained for about seven hours.

The aqueous fluorescein concentration in Group B animals was moderately reduced under acetazoleamide (fig. 6).

Group C. Animals in Group C showed little response to treatment with acetazoleamide. Following a single intravenous dose of the drug (fig. 7), there was only a moder-

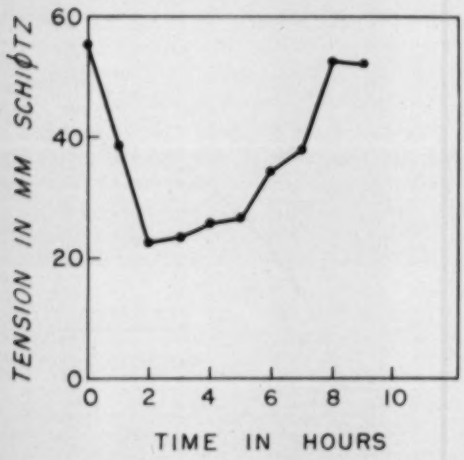

Fig. 5 (Schirmer and Ormsby). Effect of a single intravenous dose of acetazoleamide on intraocular pressure (Group B). Average values.

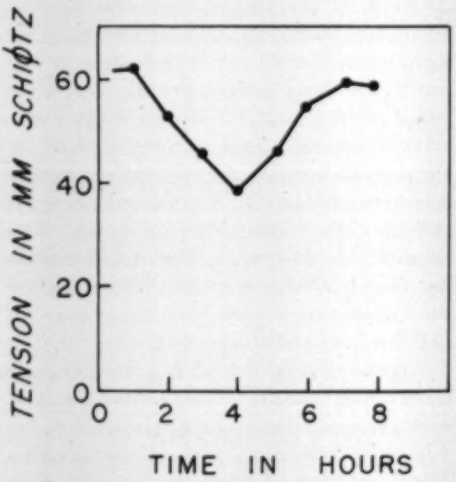

Fig. 7 (Schirmer and Ormsby). Effect of a single intravenous dose of acetazoleamide on intraocular pressure (Group C). Average values.

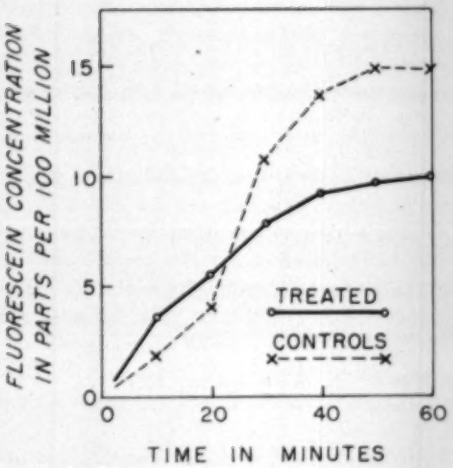

Fig. 8 (Schirmer and Ormsby). *Fluorescein test* before and after treatment with acetazoleamide (Group C). Average values.

ate lowering of intraocular pressure and this was maintained for about six hours. Fluorescein concentration in the aqueous in animals in this group was reduced under treatment with the drug (fig. 8). There was no parallelism between tension drop and protein flare, for protein continued to accumulate in the anterior chamber.

Following the instillation of 2.5-percent neosynephrine drops into the conjunctival sacs in Groups B and C, there was an average rise in intraocular pressure of three to five mm. Hg. in Group C, and none in Group B, suggesting that, in animals in Group C, blockage of the angle by protein had created a narrow-angle phenomenon.

Four of the animals in Group C eventually developed buphthalmos, whereas none in Groups A or B developed any serious sequelae.

Throughout these experiments, hyperemia of the iris, observed with the slitlamp, did not appear to be influenced by acetazoleamide.

Discussion

According to the present concept of aqueous formation, bicarbonate ions are produced by the ciliary body and actively transferred to the aqueous. The resulting increase in osmotic pressure is an important factor in aqueous production. The gradient of flow influences the penetration into the anterior chamber of crystalloids and colloids. Protein, accumulating in the interstitium of the ciliary body during inflammation, passes into the aqueous.

Acetazoleamide, by inhibiting carbonic anhydrase, decreases bicarbonate formation, thus lowering osmotic hypertension and reducing aqueous formation. With the decrease in fluid exchange it is conceivable that the passage of protein into the aqueous would be reduced. However, under acetazoleamide in the animals in Groups A and B, passage of protein into the aqueous decreased more rapidly than did fluid. The resulting decrease in aqueous colloid osmotic pressure appeared to be an important factor in the reduction in intraocular pressure.

Summary

1. Allergic iridocyclitis was induced in rabbits by the intravitreal injection of a single dose of horse serum.

2. Rabbits with iridocyclitis could be divided into three groups: Group A—those which did not develop increased intraocular pressure; Group B—those which developed increased tension which was reduced to normal with acetazoleamide; Group C—those which developed increased tension which was not controlled by acetazoleamide.

3. In *Group A*, acetazoleamide caused a decrease in aqueous protein flare and aqueous fluorescein concentration.

4. In *Group B*, acetazoleamide caused a decrease in intraocular pressure, paralleling the decrease of aqueous protein concentration.

5. In *Group C*, acetazoleamide caused a temporary slight decrease in tension, but protein concentration was not appreciably reduced.

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HEREDITARY HEMORRHAGIC TELANGIECTASIS*

With beta irradiation of a conjunctival lesion

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Review of literature

Hereditary hemorrhagic telangiectasis is a relatively uncommon disease entity known mainly to the internist, dermatologist, hematologist, and otolaryngologist. Nearly all writers on the subject mention the probability of conjunctival involvement, which is obviously extremely rare for a thorough search reveals that only one case has been reported up to now in the American ophthalmic literature.[1] There have been four reports in the European literature and, in addition, there are a few vague but suggestive references to conjunctival bleeding. There is, however, no pertinent evidence that the condition was the hereditary hemorrhagic type of telangiectasis.

Possibly the first reported case of conjunctival involvement was that of Gjessing[2] who, in 1916, described a man, aged 52 years, who had three attacks of conjunctival hemorrhage previous to systemic bleedings. This patient also had angiomas involving the face and mouth. Gjessing also reported a second case in which hemorrhagic retinopathy was the unusual accompaniment to generalized bleeding.

Mention is made of a patient seen in Jessop's Clinic in 1895 in a state of collapse from hemorrhage of an ulcerated nevus of the conjunctiva.[3] The only other recorded cases are those of François[4] in 1938, Pitter[5] in 1941, and Witmer[6] in 1951.

There have also been mentioned cases of conjunctival or lid involvement of minor nature, with no details given, but none of these cases were reported in the ophthalmic literature. Weber[7] reports two cases. Schwartz[8] reports minor involvement of one lower lid in a Negro. New and Anderson[9] report one case, and Stock[10] added two cases which presented minor conjunctival involvement. All these cases were reported because of severe recurrent epistaxis, the conjunctivas being mentioned only incidentally, with no detailed description and no mention of bleeding from the conjunctival tissues. The paucity of reports would, therefore, seem to indicate that ocular symptomatology in hereditary hemorrhagic telangiectasis is extremely rare. It may be noted, too, that hemorrhage in the retina has been recorded only twice, the first case being that of Gjessing and the second reported by Cuendet and Magnenat[11] in 1953.

Although the disease entity has been known by several names, the term most widely used in this country is hereditary hemorrhagic telangiectasis. Other terms frequently used are Rendu-Weber-Osler disease, heredofamilial angiomatosis, familial

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hemorrhagic angiomatosis, and just simply, Osler's disease. Rendu,[12] in 1896, first recognized the symptom complex and called attention to the association of familial epistaxis and multiple telangiectasis. Osler[13] described the entity in an extensive report in 1901, and Weber,[7] in 1907, added further details to complete the information as we know it today. Goldstein[14] published extensive reports on this disease and for a while after 1931 Goldstein's heredofamilial angiomatosis was the popular term. Hereditary hemorrhagic telangiectasis was first suggested by Hanes[15] in 1909, and seems to be the acceptable and logical name for this disease entity.

Characteristics of disease

Hereditary hemorrhagic telangiectasis is characterized by a number of various sized telangiectasia and angiomas which bleed spontaneously or with minimal trauma. The bleeding usually occurs from lesions in the nose but has been reported to occur from almost any portion or organ of the body. Males and females are equally affected. There are no sex-linked factors and transmission is dominant.

The typical lesion begins as a dilatation of the capillaries of a bright red color which later, as the venules become involved, changes to a violet or bluish hue. Actually, the mucous-membrane lesions are bright red, whereas the skin lesions become bluish.

The lesions make their appearance during the second decade but occasionally cases have been reported in which the lesions are seen much earlier. The earliest age of onset was reported by Dolowitz,[16] in 1953—the case of a three-months-old child. Usually, the onset of symptoms is at puberty, with a notable increase in the size and number of the lesions as the years advance. By the fourth decade, the symptoms and signs have reached their maximum and, at this time, control is frequently a trying medical problem.

Since the disease is usually manifested at puberty, its relationship to the sexual cycle seems more than a mere coincidence. Heyde[17] and Koch, Esher, and Lewis[18] have stressed the estrogen and androgen control of symptoms in their cases.

It is obvious from the literature that the most frequent site of the lesion is in the nasal mucosa and in the turbinates. Angiomas have been reported involving the larynx,[19] as well as the tracheobronchial system.[20] Skin involvement is fairly frequent and one unusual case of pulsating, stellate telangiectasis was reported by Weber.[21]

To summarize: Generally, the bleeding is from the nose but there are reports of bleeding sources from the urinary tract,[22] the finger tips,[8] and the gastrointestinal tract.[23, 24] Although bleeding from this disease is usually severe, the average mortality has been only about four percent; however, Houser[25] reports a mortality of 27.2 percent in one family.

Although the disease is considered to be hereditary, a study of the recorded cases reveals that about 20 percent have no family history of the disease. Figi and Watkins[26] reported six cases out of 20 diagnosed instances that had no positive family history. Successive transmissions through three and four generations have been reported frequently, and Dolowitz[16] had the unusual opportunity of following and tracing this disease through six generations of 491 descendants of early Mormon pioneers. His study was facilitated by the failure of these families to migrate, as well as by detailed church records. Among the 491 descendants, he found 83 bleeders.

Pathology

The pathology of the lesions was described by Neumark,[27] Fingerland,[28] and Ullman.[29] Among the microscopic findings are degenerative changes in the connective tissue which result in dilated vessels with extremely thin walls. There are many newly formed vascular buds originating from angioblasts lying in the midst of many incompletely formed blood vessels. A conspicuous deficiency of muscular and elastic layers is noted in the

vessel walls. Ullman suggests the possibility of neoplastic changes in the newly formed capillary spaces, and describes the chromatin structure of the nuclei which show an increase in number. Because the vascular walls consist of a single layer of endothelial cells, the bleeding tendency is facilitated. Hanes[15] described obliteration of the papillary layer of the corium, with resultant loss of the stratum germinativum. This, of course, produces an extremely thin layer of skin overlying the lesions and thus the tendency to spontaneous bleeding.

Diagnosis and therapy

The proper diagnosis must consider the three postulates of Hanes[15] and Larrabee and Littman[30]: (1) A history of heredity; (2) visible telangiectasia distinctly pathologic in numbers and distribution; (3) a tendency to bleed from the lesion.

The condition need not be confused with other hemorrhagic conditions, because, significantly, there is no abnormality in the blood picture other than that associated with secondary anemia. The platelet count and bleeding and clotting times are normal. The disease is distinctly nonpurpuric and nonhemophilic. Differential diagnosis must, however, consider the occasional telangiectasis seen in pregnancy, senility, and lead poisoning. Hemorrhages are also noted in cirrhosis of the liver, leukemia, and Hodgkins, Gaucher, and Banti diseases. Cordes and Hogan[31] have postulated a relationship to Von Hipple-Lindau, Sturge-Weber, and Bourneville diseases.

The multiplicity of therapeutic measures found in the literature, coupled with the paucity of uniformly good or even fairly good results, is indicative of the inadequacy of the measures available as well as the constant search for a better weapon to add to our therapeutic armamentarium. To date, no specific agent has been found and, since the most frequent presenting complaint of this disease has been epistaxis, it is not surprising to find the literature crowded with therapy directed to the nasal area.

Kindler[32] advised a bilateral window resection of the nasal mucosa, while Houser[25] successfully employed chromic-acid chemical cauterization in three of his cases. A fourth case presented satellite lesions in the immediate vicinity of the treated and destroyed lesions. These new lesions appeared within a very short period of time and showed the same tendency to hemorrhage as the preceding lesions. Occasionally septal perforations would be noted following chromic-acid cauterization but Houser felt this was preferable to nasal bleeding.

Because of the known radiosensitivity of the endothelial cells of the vascular channels, Molesworth[33] advised early radiation of these lesions, regardless of location. Weaver[34] quotes Spencer to the effect that, in his hands, high voltage X rays was effective in the treatment of hemangiomas, although increased radioresistance was noted with the increase in age of the patient. Houser,[25] on the other hand, found poor results from X rays, radium, or electrocoagulation, and preferred chemical cauterization as mentioned.

Radium has been employed successfully by Sterman and Scal,[35] while Weiss[36] described only temporary results and preferred the use of snake venom. Quick,[37] in his text on hemorrhagic diseases, quoted numerous authors who used radium as the treatment of choice in this condition; whereas, Peck,[38] Ingals,[39] and Figi and Watkins[26] feel that radium produces greater tissue friability and subsequent bleeding and, therefore, condemn its use.

Figi and Watkins[26] employed vitamin K and irradiation of the spleen but with equivocal results. Peluse[40] used vitamin C, vitamin K, and bile salts without any appreciable effect. He also employed Sylnasol, a sclerosing agent and fibrous-tissue proliferating agent without any enthusiastic results, but he found good results with the use of vitamin P. Shapiro,[41] on the other hand, felt that vitamin P was worthless.

Sclerosing solutions into the lumen of these vessels has been employed by Biege-

leisen,[42] using a microinjection technique with sodium morrhuate. Because of the obvious difficulties in this procedure, O'Kane[43] injected a five-percent solution of quinine hydrochloride and ethyl carbamate into the previously anesthetized contiguous tissues, with good results. Electrocoagulation has been employed successfully at the Mayo Clinic[26] and by Rulison.[44] The Mayo Clinic found this method of therapy the most satisfactory of all.

It is interesting to note that the formation of satellite lesions was observed by Figi and Watkins,[26] Dolowitz[16] and Houser.[25] They noted new lesions developing adjacent to the recently destroyed angiomatous lesions, irrespective of the manner in which these had been destroyed. The possibility that this form of destructive trauma might be sufficient to stimulate the formation of new angiomas, thus indicating a neoplastic rather than angiectatic origin of these vascular lesions is suggested by Stock.[10]

Electrolysis has been successfully employed by Cipollaro,[45] using the negative pole of a galvanic current as the active electrode and employing multiple punctures, the number depending upon the size of the lesion.

Good results have also been reported following the use of carbon dioxide by Fingerland and Janousek,[28] as well as by Bankoff.[46] The use of moccasin snake venom was instituted by Peck and Rosenthal[38] in 1935 and their good results in the control of bleeding was duplicated by Ingels[39] and Weiss.[36] On the other hand, Figi and Watkins[26] of the Mayo Clinic reported consistently poor results from this form of therapy.

Hormonal therapy has recently been employed successfully by Koch, Esher, and Lewis.[18] This therapy was based upon the clinical exacerbations of epistaxis noted during the periods of decreased estrogen secretion premenstrually and following X-ray castration. In male patients, they found it necessary to add methyl testosterone in order to negate the feminizing features that developed, but good results were noted in all patients. Heyde[17] reported, in 1954, the use of combined hormone therapy in one male patient with good results, but Dolowitz[16] in a very thorough and comprehensive report noted that of all the suggested therapeutic regimes none, including the most recent hormones, was efficacious in his hands.

In general, treatment has been disappointing, and the mainstay of all therapy is still blood transfusions and tamponage whenever this is possible. Radiologists and dermatologists shy away from radiation therapy because the multiple lesions expose the patient to an undesirable accumulative dosage, and because eradication of a lesion usually results in formation of a nearby satellite lesion.

In the case to be reported, the patient, a dermatologist, had given up on all treatment for this condition, particularly since his brother, also a physician, had taken a similar attitude after total erosion of the septal wall secondary to radiation. Our patient, who had had the disease for more than 30 years, would not have come into our hands except for a dramatic and alarming episode of extensive hemorrhage from the conjunctiva. This was the first episode of bleeding from the eye.

Report of case

The patient, a 60-year-old white man, a physician, had had multiple skin lesions and repeated epistaxis since the age of 30 years. On two or three occasions, he had had bleeding from the gastro-intestinal tract. During some of the episodes of bleeding, he lost sufficient quantities of blood to require blood transfusions.

On the occasion that one of us (E. E. G.) was called upon to see him, the patient was in great emotional stress and was quite agitated. He awoke on October 7, 1954, and found his entire pillow soaked in blood. There was blood on the sheets, as well as on the wall adjacent to his bed. His face was blood streaked and bloody tears came from the right eye.

When he was seen the next morning,

Fig. 1 (Garner and Grossmann). Appearance of conjunctival lesion prior to therapy.

there was a slight sanguineous appearance of the right eye and the tears in the cul-de-sac were blood tinged. The upper and lower lids of the right eye were slightly puffy and the patient seemed apprehensive about opening this eye.

Examination revealed the source of bleeding to be in the vicinity of three small bright-red lesions in the conjunctiva of the right lower eyelid. Two of these lesions were minute and measured less than one mm. in diameter, the third lesion was 2.5 mm. in diameter, and all were situated in close proximity to each other. Slight oozing of blood was noted from the larger lesion only. The upper-lid conjunctiva as well as the bulbar conjunctiva revealed no lesions. A routine examination of the eyes contributed no pertinent findings.

Fig. 2 (Garner and Grossmann). Photograph of conjunctival area April, 1955.

Fig. 3 (Garner and Grossmann). Bloody tears, O.D., with lesions (telangiectasia) of the face.

The skin of the face presented many various-sized, bluish angiomas, none of which bled. Similar lesions were noted on the nasal septum, on the thumb, and under two of his nails.

The patient is a diabetic under good control and without visual disturbances secondary to this metabolic disorder. The family history reveals no information as to his parents but does bring out a history of this disease in one older brother and sister, both alive and both having histories of repeated epistaxis and telangiectasis. Two maternal aunts are known, one of whom died from a severe, sudden gastro-intestinal hemorrhage. These two aunts had four children each and the progeny from these cousins total some 30 individuals, who have definitely been diagnosed as suffering from this malady. Most of the involved cousins and second cousins have been females.

Slitlamp examination revealed the lesions to be elevated and consisting of a network of bright red capillaries, which were tortuous and showed aneurysmal dilatations. Because there was only a slight oozing of blood from one of these lesions, immediate cauterization was not performed. Instead, a radioactive strontium-90-yttrium beta applicator with a 7.8 mm. active surface head was applied to the area for a dosage of 7,560 rep. on October 9, 1954.

No gross bleeding was noted for four days following this procedure but, on the fifth day, the patient became quite alarmed because of increased oozing of watery blood from the right eye. Inasmuch as the effects of radiation are not immediate, a light cautery was applied to the source of oozing in the larger lesion. This stopped the oozing at once.

After a period of four weeks, the appearance of the conjunctiva in the region of the lesions was entirely changed. The area of application appeared pale pink in color and was obviously lighter than the surrounding conjunctiva. Slitlamp examination revealed a marked change in the three previously described lesions in that only the larger one could be seen as a small area of increased redness while capillaries and aneurysmal dilatations could not be seen. An additional small dose of strontium-90 beta rays was recommended but the patient declined because of his general fear of radiation.

About three months later, examination revealed a normal-appearing conjunctiva in the region of the original lesions, although this area was somewhat paler than the surrounding conjunctiva. A single dilated conjunctival vessel seemed somewhat enlarged in an area about two mm. away from the site of beta-ray therapy. A coronary attack prevented us from giving this patient additional beta radiation at this time.

When last examined on March 28, 1955, the conjunctiva in the region of the original lesions appeared to be normal and flat, although slightly paler in color. The three lesions originally described no longer exist and conjunctival vessels are noted in the area. A few millimeters away from the site of therapy, a solitary larger conjunctival vessel is seen but there is no evidence of aneurysmal dilatations. It does not give the impression of a beginning satellite lesion.

Summary and Conclusion

The literature on hereditary hemorrhagic telangiectasis has been reviewed. Although repeated references are made by numerous authors concerning involvement of the conjunctiva, very few reports of cases have actually been made. There are apparently no references concerning treatment of the conjunctival aspects of the disease.

X rays and radium have proven unsuccessful in the treatment of nonconjunctival lesions because the radiation has often resulted in damage to the underlying tissues and predisposed the treated tissues to increased bleeding. For this reason it was decided to employ the Sr^{90} beta applicator, since tissue damage should be less inasmuch as the applicator's greatest efficiency is at one to two mm., the rep output decreasing to two to 11 percent at three mm. The known radiosensitivity of the lesion, as well as its superficial nature, seemed to indicate that beta therapy would not only be effective but superior to other methods of treatment. In spite of the satisfactory results in our case, it might be wise to point out that not enough time has elapsed for thorough evaluation of this form of therapy. It is unfortunate that the extreme rarity of conjunctival cases prevents an extensive trial of this therapy. It would seem worth while for the otolaryngologist to consider a beta radiation to the nasal septum in cases of hemorrhagic telangiectasis coming to his attention. Perhaps the use of beta radiation might also be evaluated in some skin lesions, especially those of recent origin.

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Ophthalmic Miniature

May 22, 1660

By the time we came on board again, news is sent us that the king is on shore; so my Lord fired all his guns round twice, and all the fleet after him, which in the end fell into disorder, which seemed very handsome. The gun over against my cabin I fired myself to the king, which was the first time that he had been saluted by his own ships since this change; but holding my head too much over the gun, I had almost spoiled my right eye.

May 23, 1660

The Doctor and I waked very merry, only my eye was very red and ill in the morning from yesterday's hurt.

Diary of Samuel Pepys.

NOTES, CASES, INSTRUMENTS

DIABETES MELLITUS WITH RELATIVE HYPEROPIA

A CASE REPORT

MORRIS ROSEN, M.D.
Philadelphia, Pennsylvania

That diabetes can affect the eye is well known. One of the poorly understood effects is on the refraction of the eye. Duke-Elder[1] reports that he investigated 43 references on the subject and myopia followed a rise in the blood sugar with a rare tendency to hyperopia. After discarding such explanations as change in the size of the eyeball, change in refractive index of the eye media, and change in accommodation, he cites a case of Elschnig's in which a patient with unilateral aphakia showed changes in refraction only in the phakic eye when the blood sugar changed. This indicated that, in this case at least, the lens was the site of the change in refraction.

Duke-Elder suggested that, because of the diuresis and loss of solids in the urine associated with an elevation in the blood sugar, the osmotic pressure of the aqueous decreased, causing imbibition of fluid by the lens cortex. By consequent increase in the curvature of the lens, myopia is encouraged. By decreasing the density of the cortex in relation to the nucleus of the lens, which does not partake in the absorption of fluid because of its sclerosis, the change at the zone of discontinuity between the two parts of the lens is greater and a ray of light passing through the lens will be deviated to a greater degree. This also tends to result in myopia.

Walsh[2] found that 21 percent of diabetics showed accommodative weakness. Duke-Elder states that accommodative changes are not important because most of the refractive changes in diabetes occur after the age of 40 years, when accommodation is decreasing, that atropine does not affect the refraction, and that astigmatic changes are common.

DeSchweinitz[3] mentioned that myopia was commonly seen in diabetes after the age of 40 years but mentioned eight cases on record in which a transitory increase in hyperopia was observed.

CASE REPORT

This is a brief report of one of the unusual results of diabetes, a relative hyperopia following an increase in blood sugar. The patient, a 42-year-old white man, had been myopic since childhood. He had had a coronary occlusion for which he had been hospitalized about two years before he consulted me. At that time, no diabetes was discovered. His glasses were about five years old and were satisfactory until a week or two before his first visit when he noted that his distant vision was poor. He was taking 14 units of insulin daily and his blood sugar (four days ago) was 150 mm. per cc.

The vision was: O.D., 6/60 corrected to 6/60 with a −5.25D. sph. ⌒ −0.5D. cyl. ax. 140°; O.S., 6/60 corrected to 6/60+1 with a −5.5D. sph. ⌒ −0.5D. cyl. ax. 90°. On being refracted, he was found to take O.D.: −3.0D. sph. ⌒ −0.5D. cyl. ax. 180° = 6/5; O.S., −3.0D. sph. ⌒ −0.5D. cyl. ax. 45° = 6/5.

Despite the fact that he understood that change in blood sugar would affect his refraction, he insisted on getting the new correction because part of his duties was driving a truck and his vision with his present glasses was too poor for safety. He promised to co-operate with his family doctor in reducing his blood sugar. His next visit was six months later, at which time he stated that his blood sugar was now normal and that he did not see well with his new glasses. A check showed that he had 6/21 vision in each eye with his new glasses, whereas he saw 6/6 or better with each eye with his old glasses.

Discussion

If we agree that the seat of the refractive change in diabetes is in the lens, one explanation for the occasional hyperopic result with rise in the blood sugar may be that the nucleus engages in hydration as well as the cortex of the lens in these cases. This would make the entire lens more uniform in density and there would be less refraction of a ray of light at the zone of discontinuity between and cortex and the nucleus.

Another explanation may be that the hyperopic changes may be due to the accommodative weakness which Walsh stated occurred in 21 percent of diabetics. While accommodation decreases with age, at 40 years a person would expect to have about 4.5 diopters of accommodation to be decreased by accommodative weakness, causing a hyperopic change. These changes are not the usual conditions one finds in diabetes, and therefore myopia occurs much more frequently than hyperopia.

744 Ritner Street (48).

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FORCEPS FOR CORNEOSCLERAL SUTURES*

Anthony Ambrose, M.D.
Newark, New Jersey

This new forceps (fig. 1) is designed for inserting the corneal side of the postplaced corneoscleral suture. The lower blade is smooth and without teeth. The upper blade has an U-shaped tip, each arm being one-mm. wide and the open space one-mm. wide. Under each arm is a single sharp tooth which fixes the corneal lip. Since the under blade is smooth, the corneal endothelium is not subjected to trauma. This solid blade flattens out the cornea and the needle is passed through easily without the cornea buckling up.

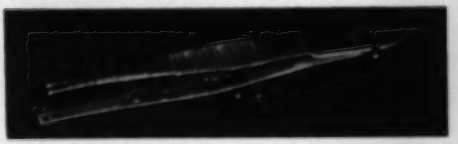

Fig. 1 (Ambrose). Forceps for corneoscleral sutures.

My technique is as follows:

Leaving the needle in place, the forceps is handed to my assistant who is ready with a Castroviejo forceps or other commonly used bipronged instrument. With this I grasp the scleral edge of the wound through which I pass the needle without first pulling it entirely out of the cornea.

15 Washington Street (2)

* Made by the Storz Instrument Company, Saint Louis, Missouri.

A DEVICE FOR OBTAINING ADEQUATE AIRWAY IN EYE SURGERY*

Max M. Kulvin, M.D.†
Miami, Florida

The problem of proper ventilation for the patient during surgery seems to have been given very little thought in the eagerness of the surgeon to carry out a meticulous and carefully planned surgical technique. Recently, one of our operating room nurses picked up a wire basket, the kind used in labora-

* From the Veterans Administration Hospital, Coral Gables, Florida.

† Chief, Ophthalmology and Otolaryngology Section.

Fig. 1 (Kulvin). The wire basket is tucked up against the patient's chin after draping.

tories to store test tubes, and asked if this would help to provide proper ventilation. On our next case we used this contrivance with success. There has been no further difficulty with aeration during surgery. Figures 1 to 3 show the manner in which these baskets are used. After the patient is draped, the wire basket is tucked up against the chin of the patient (fig. 1) The eye-drape is folded over the face and onto the wire basket in such a manner that it leaves the end uncovered but anchors the drapes to the basket and to the drapes on the body (fig. 2). The instrument tray, if it is placed over the operating table, is placed up against the open end of the basket. Figure 3 demonstrates the airway as seen from below.

1881 S.W. 36th Court (34).

Acknowledgment is made to Mrs. Everett for suggesting the basket, and to Mrs. Pitz, and Mr. A. Weinberg, medical photographer, for their help.

Since this paper was submitted for publication, a similar device has been noted in Marshall: Detachment of the Retina. London, Oxford University Press, 1936, p. 351.

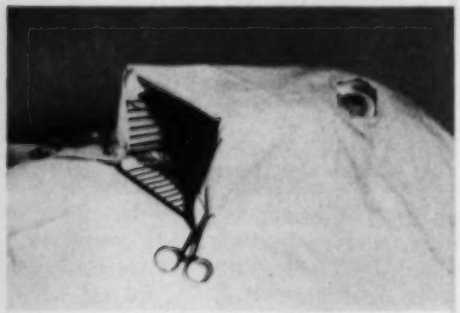

Fig. 2 (Kulvin). The end of the basket is left uncovered.

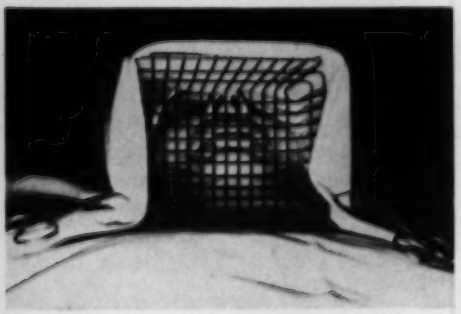

Fig. 3 (Kulvin). Front view.

GROOVED MARKING CALIPERS FOR OCULAR SURGERY*

CONRAD BERENS, M.D.
New York

A grooved marking caliper has proven satisfactory in surgery of the extraocular muscles, retinal separation, scleral resection, and other ocular procedures where accurate marking for surgery is essential.

The grooved marking calipers (fig. 1) has a set screw which permits a separation

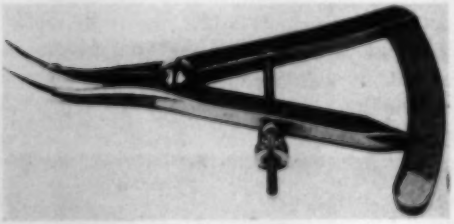

Fig. 1 (Berens). Grooved marking calipers with a separation of from one to 20 mm.

* Aided by a grant from the Ophthalmological Foundation, Inc., and the Department of Research of the New York Association for the Blind. Made by the Storz Instrument Company, Saint Louis, Missouri.

of the blades of from one to 20 mm., as measured on both sides of the rule.

The blades of the calipers are curved to a 45-degree angle, and when applied to the eyeball permits the surgeon to have an unobstructed view of the operative field.

The inner aspect of the curved tips of the calipers is grooved for holding the marking fluid (methylene blue, India ink, and so forth). Before applying the calipers to the eyeball, the tips are dipped in the marking fluid.

The marking calipers are useful in performing retroplacements of the extraocular muscles,[1,2] and in marking the sclera for the proposed application of electrolysis[3] or diathermy in operations for retinal separation, as well as for cycloelectrolysis[4] and cyclodiathermy.

708 Park Avenue.

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FIELD SCREENING TEST

JAMES MILES O'BRIEN, M.D.
Bridgeport, Connecticut

A set of visual field cards has been designed for use with a hand stereoscope.* The range and scope of these cards is of limited but definite value when properly employed. The requirements are visual acuity of at least 20/70 in either eye and binocular vision of at least first grade (simultaneous macular perception).

The main purpose of these cards is in screening field defects, especially central scotomas such as are found in early multiple sclerosis.

Supplied with the cards is a small text outlining general instructions as to their use. I have used these cards in working with neurosurgeons and neurologists during the past three years. They have been of value especially when examining hospitalized patients.

Fusion is checked by means of the large "bird in cage" card. The remaining cards cover central scotomas and manifest anopsias. The test is intended as a rapid screening method and is not meant to supplant perimetry as such.

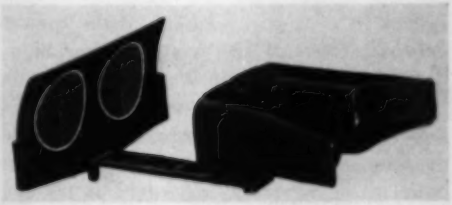

Fig. 1 (O'Brien). Equipment for field screening tests.

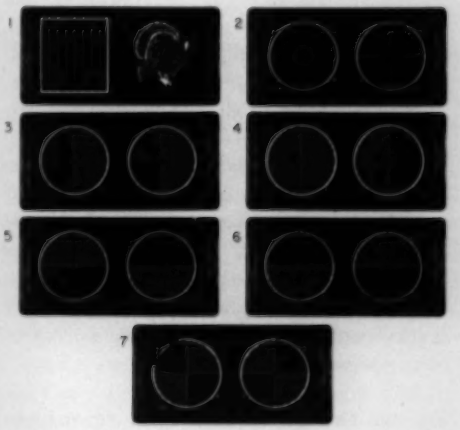

Fig. 2 (O'Brien). Visual field cards.

* The entire field screening kit is supplied at nominal cost by the Keystone View Company of Meadville, Pennsylvania.

OPHTHALMIC RESEARCH

Department

EDITED BY FRANK W. NEWELL, M.D.

Abstracts of papers presented before the East-Central Section of the Association for Research in Ophthalmology

Toronto, Ontario, January 9, 1956

V. EVERETT KINSEY, PH.D., Detroit, *Section Secretary*

Glia of the human optic nerve under normal and pathologic conditions. J. Reimer Wolter, M.D., University of Michigan, Ann Arbor.

With the improved silver-carbonate technique of del Rio Hortega it was possible to demonstrate in the human optic nerve an elaborate system of astroglia which supports the nerve fibers and surrounds the blood vessels in a manner peculiar to the central nervous system. There is also typical oligodendroglia and microglia.

It was also possible to observe the pathologic reactions of the astroglia, the oligodendroglia, and the microglia of the human optic nerve in various disorders of the eye and the brain and in tumors of the optic nerve. The main phases of the nonspecific reactions of the astroglia are: swelling and hypertrophy, proliferation, scar formation, degeneration and complete destruction. Following severe acute or chronic damage, complete break-down of all nervous and glial tissue of the optic nerve may result in replacement of both by a dense scar of connective tissue. The microglia of the optic nerve is of mesodermal origin, has phagocytic functions and forms fat-loaded "gittercells" (granular compound corpuscles) under many pathologic conditions. Typical tumors of the optic nerve are those built by primitive astrocytes or oligodendrocytes.

Diurnal changes in eosinophil count compared with those in intraocular pressure, tonographic values, and aqueous veins. Amerigo Cambiaggi, M.D., W. M. Spurgeon, Ph.D., and Richarda Spurgeon, M.A., Department of Ophthalmology, College of Medicine, University of Cincinnati.

Our objectives were to evaluate Stepanik's hypothesis of a hypophysical regulation of intraocular pressure of glaucomatous eyes, based on his findings of an inverse relation between eye pressure and eosinophil count; to compare, as did Stepanik, diurnal variations of eosinophil count with those of aqueous humor production and facility of outflow, and to study the appearance of the aqueous veins.

Statistical analysis of our data, obtained on 35 glaucomatous and 14 normal eyes, showed that our subjects fall into two groups: (I) those with significantly high correlation between eosinophil count and intraocular pressure, and (II) those with a correlation coefficient not significantly different from zero. Six of the glaucomatous eyes and none of the normal eyes fell into Group I.

Production and facility of outflow of aqueous humor did not show any correlation with eosinophil count in the normal subjects, except in one which had a significant but positive correlation for the outflow.

The tonographic values showed no correlation with eosinophil count in the glaucomatous patients, except that in two the facility and in one the production were correlated.

None of the normal eyes showed a relation between appearance of the aqueous veins on one hand, and eosinophil count and intraocular pressure on the other hand; however, such a relation was found in six of the 30 glaucomatous eyes in which the aqueous veins were studied.

It is possible that the diencephalon-hypophyseal region influences the intraocular pressure in certain cases of chronic simple glaucoma (our Group I). From our data it is not possible to explain what might be the mechanism of this influence. We can exclude the assumption that ACTH influences the ocular tension directly and the possibility that the facility of outflow of aqueous humor is primarily affected by the diencephalon-hypophyseal region.

A critical evaluation of color perimetry. Myles M. Berk, M.D., University of Pittsburgh and Eye and Ear Hospital.

The purpose of this experiment was to evaluate color as a critical factor in perimetry and to learn whether the absolute energy, independent of color, determines field size. A total of 150 central field examinations were performed with white, green, blue, and red test objects. The subjects tested were adults without color deficient vision or other ocular abnormalities.

A lighting system with a dimming control for fluorescent lamps was adapted to light the two-meter tangent screen. The energies of the fluorescent lamps with and without gelatin filters of red, green, and blue were determined with a thermopile. The energy values of the colors and the white light were set to be equal at 39 microwatts per square foot (equivalent to 12.5 foot-candles white light), so that the energies from white, blue, red, and green were equal.

Four field studies were made at each sitting, and one eye was tested at each visit. The first field was discarded, as it was found that this was always smaller than the ensuing field. The second, third, and fourth fields consisted of a color, a white of equal energy to the color, and a bright white field. The bright white light was the amount of light behind the filter necessary to transmit the color. The perception of an object rather than the discrimination of color was used as an end-point.

The use of colored and white lights of equal energies, showed the peripheral field size with green and blue light to be equal. The bright white light gave a consistently larger field, and the white lights of equal energy gave fields that were of the same size as those done with blue and green light. Red field examinations gave inconsistent results, but generally smaller field size than the blue or green. This inconsistency with red light is thought to be due to the difficulty of standardizing red light.

It was concluded that the energy of blue or green light determines the field size, rather than the color of the light, if the discrimination of an object rather than the discrimination of a color is used as an end-point. The bright white light caused the field size to be significantly enlarged as would be expected if energy rather than color determined field size.

Since color was the only variable, the conclusion drawn was that, under blue and green light, the color has no effect on field size. The decrease in field size induced by color with standard testing procedures is due to the decrease in light intensity. If this decrease is eliminated the field size will be the same whether colored or white lights are used.

The effect of epinephrine upon the rabbit electroretinogram. A. D. Ruedemann, Jr., M.D., Kresge Eye Institute, Detroit, and W. K. Noell, M.D., USAF School of Aviation Medicine, Randolph Field, Texas.

In this paper the effect of systemic epinephrine upon the rabbit electroretinogram was determined.

Six female rabbits, four albino and two pigmented, were tested, utilizing A.C. and D.C. amplifiers with simultaneous recording of electroretinogram, electroencephalogram, and electrocardiogram. The changes which epinephrine produced were mainly upon the slow wave phase of the electroretinogram and the D.C. potential across the eye. The slow wave phase is the c-wave.

Fast components, a- and b-waves, and d-

wave were primarily unaffected even in large doses (one mg.). The changes were classified into two types according to their effect upon c-wave amplitude, for example, "low dose" effect and "high dose" effect.

"Low dose" effect was obtained with intravenous injection of 0.01 or 0.1 mg. and resulted in an increase in c-wave amplitude reaching a peak in five minutes and lasting about 30 minutes. This effect was similar to that which Therman obtained with the frog.

"High dose" effect was obtained with dosage of 1.0 mg. intravenously. The amplitude of the c-wave diminished for nearly two minutes, at which time the c-wave was righted by a polarity reversed potential which lasted three to five minutes.

The effects obtained were not varied by length or intensity of stimulus.

The question of vascular effect of epinephrine was answered by (1) increased intraocular pressure, (2) air embolism causing cardiac arrest, (3) hypoxia from low oxygen concentration. In all three the c-wave amplitude diminished without being reversed.

The work of Noell would indicate that the c-wave has its origin in the area of the pigment epithelium and consists of two phases; the "active" phase caused by "active" transfer of ions across the pigment epithelium, and a "passive" phase caused by the physicochemical membrane effect of the tissues surrounding the retina.

It was concluded that the "low dose" effect of epinephrine temporarily stimulated the "active" transfer of ions while the "high dose" effect appeared to abolish directly the active phase of the c-wave for a short period of time.

Current research on the culture of lenses. Carl Wachtl, Ph.D., and V. Everett Kinsey, Ph.D., Kresge Eye Institute, Detroit.

Media were tested as to their adequacy for maintaining a normal number of epithelial cells of the lens in mitosis. Attention was directed toward the identification of those substances which were necessary to maintain normal cell division and the elimination of those substances from the media which either inhibited mitosis or caused abnormal appearance of the nuclei.

It was found that the addition of Tween in small concentration did not cause the abnormal appearance of nuclei as observed when a commercially available medium was used. The addition of fat-soluble vitamins to the KEI medium did not increase the number of cells undergoing mitosis.

By excluding some nucleosides from the KEI medium as described in earlier reports, and by substituting glutamine for glutaric acid, a medium resulted which in preliminary experiments supported normal cellular and metabolic activities of the lens for 18 hours, if the medium was replaced with fresh solution after nine hours.

Omission of all of the nonessential amino acids except cysteine, resulted in a lessening in the number of cells in mitosis. This indicates that at least in our medium, one or more of these amino acids are necessary for the support of mitosis in the lens epithelium.

Relation of luminance and duration of the visual stimulus: II. The human electroretinogram. Matthew Alpern, University of Michigan, Ann Arbor, and John J. Faris, Colorado A & M College, Fort Collins.

Measurements of the electroretinogram responses to a 7.5 degree centrally fixed white stimulus by the dilated, dark-adapted eye of one human observer are reported for a range of flash durations (five to 143 m.sec.) and luminances ($2.61\ (10)^2$ to $2.61\ (10)^6$ trolands). The apparatus has been previously described.[1] For high intensities the b-wave response to a flash longer than the action time is less than the response at the action time. For high intensities the a-wave response to a long flash is the same as the response at the action time. Thus the b-wave data compare to psychophysical data but the a-wave

1. Alpern, M., and Faris, J. J.: J. Optical Soc. Am., **44**:74-79, 1954.

data do not. The results are analyzed in terms of photochemical models[2] of the photoreceptors and for their implications for a theory of metacontrast.[3] If these psychophysical and electroretinogram results are to be explained as special examples of metacontrast then the data imply that the region of interaction in metacontrast is the synapse of the visual cells.

Radio-iodine studies on tears, aqueous, vitreous and lens. Irving Shapiro, M.D., and Arthur Solari, M.S., University of Michigan, Ann Arbor.

There is an increasing use of radio-iodine in the diagnosis and the treatment of thyroid disease. It was felt that it would be worth while to study the amount of radio-iodine found in various ocular structures of individuals receiving radio-iodine in an effort to determine more regarding the physiology of the structures concerned, and to determine if enough radiation was being directed at these ocular areas to cause future difficulty.

The study of tears in patients receiving canceracidal doses of radio-iodine suggests that there is insufficient radiation present to preclude corneal damage. Furthermore the studies suggest that iodine is not selectively secreted in the tears but directly reflects blood levels. It is felt that iodine blood levels may be adequately followed in a patient by measuring tear levels and thus avoid multiple venapunctures which are presently done. The simple method of measurement of tear levels utilizes Schirmer's technique.

Studies are now in progress to determine aqueous, vitreous, and lens radio-iodine levels both in man and animals with particular view to finding if radiation cataract is a real hazard in persons receiving radio-iodine.

The effect of hyaluronidase on the viscosity of cattle aqueous humor. J. A. Beswick, M.D., and Clement McCulloch, M.D., Toronto, Ontario.

This study is a sequel to that of Bárány (1954) in which the rate of outflow of enucleated cattle eyes was increased by the addition of hyaluronidase to the perfusing fluid. He postulated a hyaluronidase-sensitive barrier at the angle of the anterior chamber. It was thought that Bárány's observation might be due to the action of hyaluronidase on residual hyaluronic acid normally present in aqueous humor; or to a wetting action of the hyaluronidase solution, permitting a more rapid flow through the angular barrier.

An Ostwald viscosimeter pipette was used to make viscosity determinations on pooled cattle aqueous and on various control fluids. To each of these fluids hyaluronidase and a strong detergent solution were added in separate experiments, and the effect of each additive on the viscosity of the fluid was noted.

The following observations were made:

1. Hyaluronidase reduced the viscosity of vitreous solution, and of aqueous humor from stored eyes, but had no effect on the viscosity of other fluids tested.

2. The addition of detergent solution produced no change in the viscosity of any of the fluids.

It was concluded that:

1. Bárány's observations were not due to the enzymatic action of hyaluronidase on fresh aqueous humor; nor would a wetting action by the hyaluronidase solution explain his results.

2. Postmortem changes in cattle eyes permit the passage of hyaluronic acid from the vitreous to the aqueous humor.

The possibility is suggested that Bárány's results might have been due to an analogous movement of hyaluronic acid from the posterior to the anterior segment of the eye. It is not known whether a similar movement can take place in the living human.

The effect of exposure to violet and ultraviolet radiation on the absolute threshold for white light. J. C. Ogilvie, Ph.D.,

2. Wulff, V. J., Fry, W. J., and Linde, F. A.: J. Cell. & Comp. Physiol., **45**:247-264, 1955.

3. Alpern, M.: J. Optical Soc. Am., **43**:648-657, 1953.

P. J. Foley, M. A. and A. M. Crabb, M.D., Toronto, Ontario.

Subjects were dark adapted and then adapted to ultraviolet radiation for three minutes. Their absolute thresholds were measured. The procedure was repeated, replacing the ultraviolet source by a violet one of approximately equal brightness. It was found that the ultraviolet source increased the absolute threshold to white light more than did the violet source in five of the seven subjects.

The structures responsible for action potential spikes in the frog's retina. Leo E. Lipetz, Ph.D., Columbus, Ohio.

Spike action potentials were picked up from isolated frog retina by means of microelectrodes. Vital staining of the retina with methylene blue permitted simultaneous microscopic observation of the various types of retinal cells which were in contact with the microelectrode. Only when a microelectrode was in contact with the ganglion cell bodies were spike action potentials detected.

The effects of a ganglionic-blocking drug, pentapyrrolidinium, on ocular fluid dynamics. David A. Rosen, M.D., Kingston, Ontario.

Pentapyrrolidinium (Ansolysen) is a drug with a nonselective blocking action on transmission in autonomic ganglia. The experiments reported in this presentation indicate several effects of this drug on ocular fluid dynamics:

1. An inhibition of the fall in ocular pressure in the contralateral eye normally observed during tonography.

2. An inhibition of the rate of aqueous flow as calculated from tonographic tracings.

3. A flattening of the diurnal tension fluctuation curves in about 50 percent of the cases.

These data indicate a significant influence of autonomic blockade on the production and elimination of intraocular fluid.

The effect of nutritional supplements on galactose cataracts. John W. Patterson, M.D., Cleveland, Ohio.

When rats are fed a diet containing sufficient galactose, cataracts develop. The rate at which cataracts develop is proportional to the galactosemia. The importance of the high blood sugar in the production of cataracts is indicated by the fact that the lowering of the blood sugar with phlorizin will delay or prevent cataracts. That the high level of galactose produces cataracts by acting on the eye is indicated by the correlation between the development of cataracts and the blood supply to the eye. The galactose acts on the eye to produce a localized nutritional deficiency which can be reversed by adequately supplementing the galactose diet. It has been possible to determine the effective constituents in the diet and from the nature of these substances to draw certain inferences regarding the mechanism by which galactose cataracts are produced. These studies also provide information regarding the biochemical mechanisms by which the normal lens obtains its energy. The findings are consistent with a system in which the glycolytic and tricarboxylic acid cycle pathways are functional.

Oxidative phosphorylation in ciliary processes. Morton B. Waitzman, M.S., Ph.D. and Elmer J. Ballintine, M.D., Cleveland, Ohio.

It has been known for several years that the ciliary epithelium contains dehydrogenases and the cytochrome system capable of oxidizing dicarboxylic acids with molecular oxygen. The ciliary process stroma lacks the cytochrome system. This separation of metabolic systems by a membrane capable of being oxidized and reduced is thought to be the fundamental anatomic arrangement responsible for the production of an excess of bicarbonate ions in the aqueous humor.

Certain cyanine and Styrylquinoline dyes, in high enough concentration, inhibit the cytochrome oxidase system. After intracarotid injection of appropriate amounts into

albino rabbits, these dyes concentrate in ciliary epithelium where they inhibit the oxygen consumption of the ciliary process in about 50 percent of the animals. In all treated eyes, the intraocular pressure was lowered, even though the oxygen consumption was normal. It was concluded that the dyes were lowering the intraocular pressure by a mechanism different from, or in addition to, their direct effect on the cytochrome system. The demonstration that these dyes in lower concentration uncouple oxidation from phosphorylation suggested that oxidative phosphorylation might be involved in the observed lowering of intraocular pressure. Therefore, methods were developed for the measurement of oxidative phosphorylation of ciliary processes.

The presence of endogenous adenine nucleotide and orthophosphate in the tissues was demonstrated by paper chromotographic separation of concentrated protein-free supernatants.

Oxidative phosphorylation in homogenates of pigmented ciliary processes, liver and renal cortex, was measured using a modification of the method of Krebs et al. (Biochem. J., **54**:107, 1953), in which the rate of appearance of radioactive phosphorus in adenine nucleotides was determined.

The experiments indicate that oxidative phosphorylation enzyme systems are active in the approximate order of magnitudes of 8:5:1 in rabbit liver, rabbit renal cortical and hog pigmented ciliary processes, respectively. A similar order was observed for O_2 uptake. Phosphorylation quotients were in the order of 2, 2 and 3, respectively.

When the homogenates were incubated under certain conditions, orthophosphate accumulated. These conditions were: (1) addition of Styrylquinoline dye #863 to the liver, kidney, and pigmented processes systems; (2) homogenizing the tissues with the Waring blender; (3) using nonpigmented ciliary processes from albino rabbits.

This accumulation of orthophosphate appears to be a result of imbalance in the phosphorylating and phosphorolytic enzyme systems, such that the latter system predominates either because of inhibition, destruction, or subthreshold concentrations of the former system, or because of a potentiation of phosphorolysis.

As a result of the orthophosphate accumulation the calculation of Krebs and of Bartley and Weber for finding turnover rates could not be applied. When equations were derived that could be solved for the rates of phosphorolysis and phosphorylation, the solution depended on small differences between larger numbers representing specific activity of the adenine nucleotides and the orthophosphate. Small errors in B-emission counting, therefore, may cause large errors in the calculated rates. Attempts to increase the precision of counting and investigation of the role of ADP and AMP in the reaction complex are now being undertaken.

On the presence of condensing enzyme in mammalian lens. Irene Karkas, M.A., and Albert Potts, M.D., Cleveland, Ohio.

The exact pathway by means of which the lens attains its energy production is still open to question. There is particular doubt about whether the avascular lens in its medium of aqueous humor has an adequate oxygen supply to operate a tricarboxylic acid cycle type metabolism. Evidence both for and against such a mechanism has been published in the past. One contribution to the controversy can be made by demonstrating the presence or absence of the enzymes necessary to carry on such a system. Some years ago Ely demonstrated the action of lens on a number of typical tricarboxylic acid cycle substrates. However, there was no demonstration of the presence of the condensing enzyme. This enzyme, which condenses a 4-C particle with a 2-C particle to create a 6-C tricarboxylic acid and reinitiate the cycle, is the focal point for the tricarboxylic acid cycle and essential for its operation. Using the sensitive method of Natelson *et al.* for determination of citrate, we have been able

to demonstrate the condensation of oxaloacetic acid with acetyl coenzyme A to form citrate, catalyzed by lens. Whereas this does not conclusively prove that the tricarboxylic acid cycle is utilized in the metabolism in the lens, it does demonstrate in conjunction with the work of Ely that all the necessary enzymic components are present for such a system to operate.

On the ophthalmotonic consensual reaction and its relationship to aqueous dynamics. Emile L. Prijot, M.D., and Howard H. Stone, M.D., Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital, Baltimore, Maryland.

The purpose of this study was three-fold: (1) To re-examine the ophthalmotonic consensual reaction in humans and rabbits; (2) to explore some of the factors involved in the mechanisms of this reaction; (3) to study pharmacologic agents which might alter the ophthalmotonic consensual reaction. Seventy normal human subjects and 73 rabbits were studied.

The conclusions were: (1) When clinical tonography is performed on a pair of human eyes, the second eye usually shows a lower initial intraocular pressure (Po) than does the first. (2) With respect to rabbits it was established that after compression of one eye the intraocular pressure in the other fell. This fall was associated with a reduced flow of aqueous humor and a normal coefficient of the facility of outflow, a normal episcleral venous pressure and normal ocular rigidity. (3) No fall in intraocular pressure and no reduction of flow in the second eye were observed when the animals were systemically atropinized. This finding suggests that the parasympathetic nervous system may participate in the ophthalmotonic consensual reaction.

Measurements of aqueous outflow in enucleated eyes. Edward W. Purnell, A.B., Carlton B. Melton, Ph.D., and Elliott Q. Adams, Ph.D., Western Reserve University, Cleveland, Ohio.

In order to study the characteristics of aqueous outflow in the absence of aqueous production, vascular changes, and extraocular influences, experiments were performed on enucleated cat eyes. The amount of infusion fluid required to maintain the eye at a constant pressure was measured by a specially designed flowmeter, which served both as a constant level reservoir and as a variable resistance in one arm of a modified Wheatstone bridge. Pressure was simultaneously recorded by means of an electronic monometer. Some eyes were brought to experimental pressure by way of the anterior chamber, others by way of the vitreous compartment.

With this system the apparent rate of outflow increased with time after cannulation; the change appeared to be less marked in eyes brought to experimental pressure by way of the vitreous compartment.

Measurements from the anterior chamber showed that electrical stimulation of the autonomic nerve supply caused a transient increase in intraocular pressure, and a reflux of infusion fluid back through the flowmeter, presumable because of a decrease in ocular volume. In some eyes there were changes either in outflow through the anterior chamber during stimulation, or in ocular volume following it. Experimental procedures to separate volume changes from changes in resistance to outflow are being investigated.

It was also demonstrated in eyes brought to pressure by way of the anterior chamber that electrical stimulation could cause an increase in capacity of the vitreous compartment, accompanied by a diminution in the size of the anterior chamber. This, the authors feel, can be explained by forward movement of the lens to a more physiologic position, assisted perhaps by an alteration in zonular tension during stimulation.

It seems most probable that these pressure volume effects are mediated through the ciliary muscle; and that in vivo, they may be

as important as local vascular changes in explaining pressure rises seen during stimulation of autonomic pathways.

Eye movements in an adult with cerebral hemispherectomy for tumor. David Volk and Jan H. Bruell, Cleveland Heights, Ohio.

A 39-year-old man developed a malignant tumor in the right cerebral hemisphere. A right hemispherectomy was done. The incision extended through the corpus callosum. The globus pallidus, putamen, and caudate nucleus were removed, as well as a considerable portion of the thalamus. All that remained was the medial thalamus and brainstem.

The patient made a remarkable recovery and survived five months, at which time regrowth of the tumor caused his death. Postoperatively he was found to have superior intelligence (verbal I.Q. of 125), and was completely lucid and co-operative. Five weeks prior to his death, numerous visual function tests were performed. Among the results obtained were normal voluntary gaze in all directions, and normal convergence. When the patient was placed in a completely darkened room and asked to look straight ahead, the head would turn 25 degrees towards the side opposite the hemispherectomy, the eyes remaining in the primary position with respect to the head. If, in the darkened room, an assistant held the patient's head in the straight forward position, the eyes would turn 25 degrees towards the side opposite the hemispherectomy.

The clinical relation between uveitis and acute upper respiratory infection. James G. Fowler, M.D., Buffalo, New York.

A review of 156 attacks in 124 consecutive cases of uveitis seen in private practice showed the etiologic factors to be as follows: focal infection 29 percent, tuberculosis 6.5 percent, arthritis 5.6 percent, syphilis 4.8 percent, gonorrhea 3.2 percent, virus infection (severe bilateral cases) 3.2 percent, diabetes 2.4 percent, sarcoid 0.8 percent, metastatic 0.8 percent, and undetermined 46.8 percent. Of the 156 attacks 31.4 percent were preceded or accompanied by acute upper respiratory infection. The diagnosis of focal infection must be a presumptive diagnosis in most cases and the same can be said of tuberculosis and lues. No case of brucellosis was encountered. Comparison of these etiologic factors with those published by Gifford in 1930 shows a decrease in lues and tuberculosis and an increase in the number of unknowns. The incidence of arthritis, gonorrhea, and diabetes was about the same. Acute upper respiratory infection deserves more attention as an etiologic factor in uveitis. Iris atrophy after a mild attack of uveitis, and recurrences in the same eye similar to the recurrences of herpes labialis and dendritic ulcer, would point to direct invasion by a virus rather than allergy. New techniques in culturing aqueous humor might throw more light on this problem.

Color photography through the slitlamp microscope. Jack H. Prince, Department of Ophthalmology, University Hospital, Columbus, Ohio.

Color photography through the slitlamp microscope has always been difficult because most of the available light passes through the cornea and lens instead of being reflected back to the camera. A long exposure has therefore been necessary. Several workers have made successful pictures with exposures of the order of one second or more. This is not useful with patients of low intelligence or poor fixation, or when the pupil is active. Instantaneous exposures of not less than one twenty-fifth of a second are essential.

A Xenon gas lamp was adapted to a Haag Streit slitlamp, as described by us, using the Zeiss Nordensen Retinal Camera (Arch. Ophth., **53**:267, 1955), to produce Kodachrome transparencies of high quality of the cornea, lens, iris, and sclera at speeds of one twenty-fifth second and less. New lenses are being computed to improve this quality and

it is hoped that eventually almost any pathologic condition may be photographed at speed in color.

A hand sorted punch card for eye research literature. Albert M. Potts, M.D., Cleveland Ohio.

Due to the geometrically expanding rate of appearance of publications in medical and allied fields, previous methods of information storage prove to be no longer adequate. The present paper describes the design and use of a hand sorted edge-punched card which makes stored information immediately available at any time after the information has been recorded. It is to be emphasized that no more information can be obtained from such a system than is put into it. However, with the increased volume of references necessary for writing scientific papers, reviews, or monographs, some such system will eventually become universally necessary. Suggestions for adaptation to specific applications will be made during the presentation.

Improved all-glass telescopic and microscopic spectacle lens. David Volk, Cleveland, Ohio.

The telescopic and microscopic units described are essentially Galilean telescopes, consisting of a positive objective lens and a negative eyepiece lens separated by air. The improvements over present telescopic spectacle lenses consist in:

1. No special mounting is necessary for the components. By using the proper base curves, the necessary refraction and separation of the optical elements of the telescope is obtained while the carrier portions of the two elements meet at an edge which can be inserted into a standard plastic or metal frame.

2. The nontelescopic carrier portion of the unit is visually useful allowing "visual field" surrounding the magnified image seen through the telescopic portion.

3. The unit is relatively light in weight. The elimination of extra carriers for the lenses tends to decrease weight.

4. The unit is cosmetically superior to any available telescopic spectacle. The appearance is similar to a cataract lens.

Effects of polyethylene tubing to obstruct the chamber angle in rabbit eyes. Frank A. Vesey, M.D., Toledo, Ohio.

No progress has been made so far to settle the differences between the mechanical and physiopathologic concepts concerning the origin of glaucoma. To decide the importance of the structures of the chamber angle in the generation of increased intraocular pressure, it seemed that obstruction of the angle by purely mechanical means would prove or disprove the theories of mechanical concept.

It has been considered that fine polyethylene tubing would be a suitable material for such obstruction. Animal tissues tolerate this foreign matter rather well and the gentle spring-action of the circularly bent straight tubing would be just enough to exert pressure and obstruct by bulk without compression. Tubing of 0.6 and 0.9 mm. outside thickness was sterilized by soaking in 1:1,000 Zephiran solution and rinsing and soaking in sterile water. Three to 12-months-old animals of mixed breed were used.

A keratome incision five mm. long was made two to three mm. inside the limbus and parallel with it. The folded but not broken tubing was introduced between the iris and cornea and released to adapt itself into the chamber angle. The length of tubing was measured to match the entire circumference of the chamber angle. The released tubing was observed promptly creating an insert exactly conforming with the chamber angle. The corneal wound was closed by three to four fine black silk corneal sutures. Intraocular pressure was taken before and after operation in both eyes, the second eye being used as control during the experiments. It was from here on recorded at irregular intervals, the animal being observed from three to 12 months, then killed. The visible changes of the eyes were recorded and occasional color

photographs were taken during the course of experiments. Pathologic sections were prepared after killing of the animals.

The most significant observation in all these experiments was the absolute lack of elevation of intraocular pressure at any time. The consistent finding was an immediate drop to zero or up to 4.0 mm. Hg immediately following surgery. The pressure rose to 8.0-12.0 mm. in a few days and up to normal in one or two cases only. It remained about half of normal in the majority of cases during the whole period of observation.

An interesting observation was the development of a dark crimson ring of dense vascularization, two to three mm. wide, occupying the periphery of the cornea and leaving the central part clear. This vascular ring developed in three to six days and cleared up in a few weeks. After this period the eyes looked and behaved entirely normal, in spite of the complete blocking of the whole of the chamber angle.

These experiments seem to prove that obstruction of the angle alone has nothing to do with increased intraocular pressure in rabbits.

Preliminary studies on the effect of Diamox on ascorbic-acid levels in aqueous humor. T. H. Hodgson, M.D., and S. Hennighausen, B.A., Toronto.

The carbonic anhydrase inhibitor, Diamox, was administered to rabbits intravenously and the effect on the concentration of ascorbic acid in the aqueous humor noted at various time intervals. A sharp drop in the intraocular pressure was noted at the 15-minute interval and although the tension returned to normal in about one hour, there was no significant change in the ascorbic acid content in the aqueous humor up to two hours after the injection of Diamox.

Experiences with APC infections in the summer of 1955. Frances Doane, B.S., A. J. Rhodes, M.D., and H. L. Ormsby, M.D., Toronto.

Following the demonstration, in Toronto, earlier in 1955, of APC Type 3 virus in the conjunctival secretions of adult patients with keratoconjunctivitis, an intensive survey of children's eye infections was made during the summer and fall of 1955.

Eye washings were taken from over 50 patients with acute follicular conjunctivitis, and isolation of APC viruses on HeLa cells grown in roller tubes was successful from a number of these. Symptoms in children consisted of sore eyes, sore throat, fever, malaise, and muscle pains. Catarrhal otitis media was a common complication. The conjunctivitis occurred usually in one eye but frequently spread to the other after an interval of three to five days. Preauricular adenopathy could usually be elicited during the acute phase but was seldom prominent. Submaxillary and generalized adenopathy was occasionally observed.

Corneal involvement was not seen in children but this could be due to the fact that it was seldom possible to get a follow-up examination of children once they had recovered. In adults, however, corneal opacities of the so-called "minor" type were frequently seen, and in some patients there was a moderate reduction in the visual acuity.

Typing of isolated viruses revealed that some of these belonged to the APC Type 3. A number of strains were not neutralized by Type 3 antiserum. The epidemic therefore would appear to have been caused by more than one type of APC virus.

Aqueous humor outflow: An experimental study using radiopaque materials: I. Injection technique, response evoked, and demonstration of pathway of outflow. Bruce E. Cohan, B.S., Ann Arbor, Michigan.

Because of the difficulties encountered in the use of particulate radiopaque substances in earlier studies of the pathway of outflow of aqueous humor, the present experiment employed three water-soluble, nonparticulate radiopaque compounds.

The injection technique used was a modification of the method of Amsler and Verrey. Two 30-gauge needles, attached to tuberculin syringes, were directed in an oblique, "sclera-splitting" course into the anterior chamber of anesthetized albino rabbits. After aspiration of 0.3 cc. of aqueous into one syringe, an identical volume of the radiopaque materials was introduced from the second syringe. The control eyes underwent the same procedure except that the radiopaque material was not instilled.

Both control and test groups responded to the procedure with a transient rise in intraocular pressure as indicated by serial tonometer measurements. On slitlamp examination all eyes exhibited dilatation of the iris vasculature, iris edema, and aqueous flare. Early formation of posterior synechias was observed within a few hours after instillation of the radiopaque material in many of the test eyes. These synechias cleared completely without treatment within a few days to two weeks, a somewhat longer period than that required for disappearance of vessel dilatation and flare. Repeated instillations of the substances into the same eyes after recovery resulted in identical responses. Histologic examination of specimens taken at intervals varying from soon after instillation of the materials to six weeks postinstillation failed to reveal the presence of any ocular foreign substance. There was no histologic evidence of an active inflammatory process at any time. It is felt that both control and test eyes exhibited the iris-stroking response described by Duke-Elder and Duke-Elder, but that, in the slightly more responsive test group, there was probably a mild chemical iritis superimposed.

Serial X-ray films of the eyes, undisturbed except for the instillation of the radiopaque media, were obtained by a relatively simple roentgenographic technique.

They demonstrate the anatomy of the aqueous chamber including the minute structures at the angle which are concerned with the outflow of aqueous humor. The earliest films demonstrate anterior chamber well filled with the radiopaque material; the angle is sharp. Moments later, a film of the same angle reveals filling of the "ciliioscleral sinus," the rodent equivalent of the canal of Schlemm in higher mammals. A film exposed a short time later demonstrates roentgenographically the outflow of radiopaque material through the aqueous veins. The veins are seen to begin just anterior to the angle and flare backward to the episcleral venous meshwork where the contents are rapidly diluted with blood. In subsequent films there is filling of both the anterior and posterior chambers as a result of diffusion of the radiopaque substance behind the iris.

Research grants awarded by the Public Health Service during 1954*

California

Los Angeles, University of California

Crescitelli, F.: Comparative study of retinal pigments, $11,394.00; Irvine, S. R., and Selle, W. A.: Surgery of detached retina, $11,266.00; Lindsley, D. B.: Mechanism of vision in man and animal $20,835.00.

San Francisco, University of California

Hogan, M. J.: Investigations on ocular toxoplasmosis, $9,367.00; Hogan, M. J.: Study of the action of lytic enzymes on the cornea, $8,968.00.

Colorado

Denver, University of Colorado

Thompson, R.: Local antibody production in the rabbit's cornea, $4,492.00.

* During the fiscal year ending June 30, 1954, the Public Health Service awarded 2,855 research grants in the amount of $29,951,150.00. Three hundred of these grants were by the National Institute of Neurological Diseases and Blindness and $2,826,033.00 was approved for payment. The information herein was abstracted from Public Health Service Publication No. 423. Only grants appearing to be of specific interest to workers in ophthalmology have been listed.

CONNECTICUT

New Haven, Yale University

Stone, L. S.: Regeneration of retina and lens, $10,000.00.

DISTRICT OF COLUMBIA

Washington, Georgetown University

Patz, A.: Oxygen administration in retrolental fibroplasia, B-$11,539.00; C-$2,397.00.

ILLINOIS

Chicago

Michael Reese Hospital

Kagan, B. M.: Co-operative study on retrolental fibroplasia, $1,890.00.

University of Chicago

Polyak, S.: The vertebrate visual system, $6,642.00; Wright, F. H.: Co-operative study on retrolental fibroplasia, $250.00.

University of Illinois

Stillerman, M. L.: Electroencephalographic findings in strabismus, $2,381.00.

INDIANA

Bloomington, Indiana University

Day, H. G.: Conversion of carotene to vitamin A, $6,015.00.

Indianapolis, Indiana University

Summers, W. A.: Growth requirements of Toxoplasma gondii, $3,564.00; Schlaegel, T. F., Jr.: Electroencephalographic findings in strabismus, $1,000.00; Schlaegel, T. F., Jr.: Conditioning in hysterical amblyopia, $6,316.00; Schlaegel, T. F., Jr.: Studies on toxoplasmic uveitis, $8,100.00.

IOWA

Iowa City, State University of Iowa

Burian, H. M.: Electric responses of the human visual system, $17,334.00; Janes, R. G.: Diabetic cataract and vascular abnormalities, $6,085.00.

LOUISIANA

New Orleans

Louisiana State University

Barber, A. N., and Ronstrom, G. N.: Development of the human visual pathway, $3,850.00.

Southern Eye Bank

Haik, G. M.: Co-operative study on retrolental fibroplasia, $9,150.00.

Tulane University

Allen, J. H.: Ocular involvement in visceral Larva migrans, $8,788.00.

MARYLAND

Baltimore, Johns Hopkins University

Friedenwald, J. S.: Study of diabetic retinopathy, $18,000.00; Friedenwald, J. S.: Enzymatic histochemical studies on ocular tissues, $8,775.00; Kuffler, S. W.: Physiology of the visual system, $17,361.00; Woods, A. C.: Etiology and treatment of uveitis, $12,528.00.

MASSACHUSETTS

Boston

Boston Lying-in Hospital

Smith, C. A., and King, M. J.: Cooperative study on retrolental fibroplasia, $1,798.00.

Harvard University

Grant, W. M.: Actions of chemicals injurious to eye or vision, $9,720.00. Balazs, E. A.: Hyaluronic acid in the vitreous body, $12,423.00; Cogan, D. G.: Study of eyes in identical and fraternal twins, $6,480.00; Grant, W. M.: Pressure-regulating mechanisms in glaucoma, $13,172.00; Jakus, M. A.: The fine structure of fibrous components of the eye, 8,293.00; Vargas, L.: Properties of multicomponent gels, $7,850.00.

Cambridge, Harvard University

Wald, G.: Chemistry of rod vision, $6,680.00.

Individual

Forbes, A.: Electric response of vertebrate retina to color shift, $4,000.00.

MICHIGAN

Ann Arbor, University of Michigan

Scharenberg, K., and Fralick, F. B.: Normal and pathologic neurohistology of the eye, $7,560.00; Wilson, J. L.: Plasma oxygen tension in retrolental fibroplasia, $4,000.00; Wilson, J. L.: Plasma oxygen tension in infants, $6,000.00.

Detroit, Kresge Eye Institute

Kinsey, V. E.: Study on retrolental fibroplasia, $18,070.00.

MINNESOTA

St. Paul, Minnesota Division of Social Welfare

Willerman, E. G.: Effect of parental attitudes on behavior of blind children, $11,382.00.

MISSOURI

St. Louis

Jewish Hospital of St. Louis

Blumenthal, H. T.: Degeneration of cerebral and retinal arteries, $7,938.00.

St. Louis University

Hanlon, C. R., Wyatt, J. P., and Szewczyk, T. S.: Experimental studies of anoxia, $5,670.00.

Washington University

Lowry, O. H.: The quantitative histochemistry of the retina, $6,000.00.

NEW YORK

Ithaca, Cornell University

Murray, E.: Color vision cross-test standardization, $5,400.00.

New York City

Columbia University

Frantz, V. K., Kligerman, M. M., and Quimby, E. H.: Thyroid cancer caused by radiation, $3,888.00; Lowenstein, O.: Electronic method for direct pupillography, $12,960.00; Silverman, W. A.: Co-operative study on retrolental fibroplasia, $367.00; Smelser, G. K.: The differentiation of ocular tissues, $10,107.00.

Cornell University

Engle, M. A.: Co-operative study on retrolental fibroplasia, $733.00; Landesman, R.: Conjunctival circulation in pregnancy, $666.00.

The Eye Bank for Sight Restoration, Inc.

Teng, C. C.: Anatomic studies of the pheripheral retina, $9,300.00.

Fordham University

Misiak, H.: Critical flicker frequency, $1,674.00.

The Home for Aged and Infirm Hebrews

Kornzweig, A. L.: The eye in old age: A clinical and pathologic study, B-$2,724.00; C-$12,000.00.

Mount Sinai Hospital

Bender, M. B.: Effects of cerebral lesions upon visual perception in man, B-2,829.00, C-$12,000.00; Bender, M. B.: Oculomotor pathways in the brainstem, $15,174.00.

New York Medical College

Haig, C.: Spectral sensitivity in night blindness, $540.00.

New York University

Lanman, J. T.: Co-operative study on retrolental fibroplasia, $265.00.

Rochester, University of Rochester

Boynton, R. M.: Chromatic adaptation and stray light in the visual system, $4,050.00; Peskin, J. C.: Carotenoid and protein components of the visual receptor system, $2,700.00; Snell, A. C., Jr.: Inflammatory reactions of the iris to injury, $1,200.00.

Syracuse, Research Foundation of State University of New York

Feldman, H. A.: Toxoplasma in human disease, $8,213.00.

NORTH CAROLINA

Winston-Salem, Wake Forest College

Roberts, R. W.: Glaucoma study. $3,500.00.

OHIO

Cincinnati, University of Cincinnati

Ascher, K. W.: Aqueous-veins research, $7,500.00.

Cleveland

University Hospital of Cleveland

Kennell, J. H.: Co-operative study on retrolental fibroplasia, $1,020.00.

Western Reserve University

Ballantine, E. J., and Melton, V. D.: Secretory mechanisms of the ciliary body, B-$6,496.00, C-$5,653.00; Brecher, G. A.: Innervation of the ciliary body, $12,534.00, Johnson, L. V.: Nutrition and metabolism of the eye, B-$7,999.00; C-$1,321.00; Patterson, J. W.: Diabetic cataracts, $11,241.00; Potts, A. M.: Experimental and clinical study of electroretinography, B-$12,486.00, C-$1,795.00; Potts, A. M.: An experimental study of the toxic amblyopias, $11,736.00.

Columbus, Ohio State University

Cole, C. R.: Toxoplasmosis in animals and man, $7,000.00; Culler, A. M.: Visual screening tests, $1,836.00; Culler, A. M.: Immunology of aqueous humor, $5,076.00; Shaffer, T. E., and Battles, M. L.: Co-operative study on retrolental fibroplasia, $1,333.00.

OKLAHOMA

Oklahoma City, University of Oklahoma

Schneider, R. A.: Effect of photic flicker on A-V oxygen differences and tissue oxygen tension, $5,794.00.

OREGON

Portland, University of Oregon

Harris, J. E.: Metabolism of the lens and cornea, $8,500.00.

Abington, Abington Memorial Hospital

Wilder, T. S., and Shelly, R. M.: Co-operative study on retrolental fibroplasia, $840.00.

PENNSYLVANIA

Philadelphia

Jefferson Medical College

Pincus, I. J., Town, A. E., and Naidoff, D.: Ocular and chemical changes in alloxan diabetic animals; Town, A. E.: Radioactive phosphorus and ocular tumor, $3,607.00; Wagman, I. H., Waldman, J., and Naidoff, D.: Retinal sensitivity in the normal eye, $10,125.00.

Temple University

Kendall, N.: Co-operative study on retrolental fibroplasia, $1,868.00.

Wills Eye Hospital

Leopold, I. H.: Corticosteroids in the aqueous humor, $14,000.00.

Pittsburgh

Elizabeth Steel Magee Hospital

McCluskey, E. R.: Co-operative study on retrolental fibroplasia, $300.00.

Eye and Ear Hospital

Wolken, J. J.: A study of photoreceptor structures in biological systems, $10,425.00.

University of Pittsburgh

Linn, J. G., Jr.: The development of diabetic retinopathy, $4,473.00; Reyer, R. W.; Experimental study of lens induction in amphibians, $3,807.00.

TEXAS

Galveston, University of Texas

Gingrich, W. D.: Ophthalmic bacteriologic and therapeutic studies, $3,024.00; Russell, W. O., and Wynne, E. S.: Ocular squamous-cell carcinoma in bovines, $10,152.00.

VIRGINIA

Charlottesville, University of Virginia

Speidel, C. C.: Experimental modification of nerves and sense organs, $2,376.00.

SOCIETY PROCEEDINGS

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This joint meeting was conducted as a symposium on "Retinal detachment."

MODERATOR: Dr. John M. McLean, New York. PANEL: Dr. Graham Clark, New York; Dr. Charles L. Schepens, Boston; Dr. Donald M. Shafer, New York; and Dr. James S. Shipman, Philadelphia.

DR. MCLEAN: *Dr. Clark, in which cases would you use a scleral resection as a primary procedure? Why are scleral shortening operations better than classical diathermy for these cases?*

DR. CLARK: For the purposes of this discussion all detachments may be divided into three categories:

1. *Simple detachments* or those which will reposition themselves on removal of the subretinal fluid.

2. *Complicated detachments* or those in which mechanical forces such as retinal shrinkage, surface membranes, persistent strong vitreous traction, or agglutinated retinal folds prevent the retina from repositioning itself against the wall of the eye.

3. *Borderline* or *doubtful* or those in which the surgeon does not have sufficient evidence to put them in the first two classes or those under weak vitreous traction which, while allowing the retina to get back to the wall, will, by the persistence of its pull, redetach it.

In Classes 2 and 3 scleral shortening is the procedure of choice and when indicated should be the primary procedure, for there is ample evidence that the diathermy reaction causes retinal and vitreous shrinkage and may not only convert a simple detachment into a complicated one but may put a complicated one beyond the reach even of the scleral shortening operation. In addition, it causes scleral necrosis and makes the scleral shortening procedure difficult or impossible in that area for a period of two or three months.

In these latter two groups are the detachments in aphakia and high myopia and those of long standing, as well as those characterized by foamy equatorial ridges and multiple holes and those with angular holes whose edges are stiffly everted, but these surface characteristics are not sufficient criteria in themselves.

The decision must rest on the most complete knowledge of the mechanical factors involved. A period of repeated observations with the patient resting comfortably in bed with the eyes bandaged for 48 hours should be a minimum.

DR. SCHEPENS: Dr. Clark tells us that cases which belong to Class 1 should be treated by simple diathermy. However, it is my experience that there are instances when a detachment appears favorable preoperatively but reacts very poorly to a correctly applied diathermy treatment. I am often unable to classify a case until after it has been operated upon, and that is of limited practical usefulness. Consequently, a choice of operative procedure which is based on the appearance of the detachment must lead to many disappointments. The only logical course therefore is to treat every case as if it were unfavorable.

As far as the classification itself is concerned, I agree that the presence of aphakia or high myopia may be important; however, in my opinion, the existence of fixed retinal folds is of such overwhelming importance that this should be the deciding factor in classification. There are cases with aphakia or high myopia which do extremely well, but all cases tend to do poorly once they have fixed retinal folds.

I strongly agree with the statement that extensive diathermy greatly diminishes the chances of reattachment. Therefore it is extremely important to apply the treatment as gently as possible.

DR. SHAFER: There is one point I should like to mention: I cannot see why any procedure that is likely to convert a so-called Class 1 into a Class 2 or 3 case should be utilized at the outset if there is available some procedure which is less likely to end up as a Class 3 case. I would feel that a less destructive or involved primary procedure might save a certain number of cases from being converted from Class 1 into Class 2 or Class 3.

DR. SHIPMAN: I must say I am not too overwhelmed by the fear of too much diathermy. To my knowledge I have only seen a single eye that was destroyed by using too much diathermy, and that was many years ago. Personally I feel diathermy is still the major weapon to use against retinal detachment and, if I had my choice of diathermy or resection, I would take diathermy. I still rely chiefly on this, even though I do resection. I might not use as strong a current as I would otherwise but, first of all, I put Walker pins in for real insurance in holding the retina. The criteria for resection are as have been expressed by other members of the panel. If the retina does not go back into place within five days, I do a resection. I think we must allow more than 48 hours. That is the criterion I go by.

DR. MCLEAN: *Dr. Schepens, what are the advantages of scleral buckling with a plastic implant over classical diathermy or scleral resection?*

DR. SCHEPENS: A scleral buckling operation generally consists of the following steps:

1. Adequate exposure of the sclera.
2. Localization of all the retinal breaks by ophthalmoscopy, a mark being made over each break on the sclera with a flat diathermy electrode.
3. Excision of a scleral lamella four to six mm. in width, and one to three quadrants in length. It is essential that the middle of the excised strip of sclera should be slightly posterior to the retinal breaks. However, when the breaks are anterior to the equator, the middle of the excised strip should be placed at the equator.
4. The area of scleral excision is covered with surface diathermy.
5. Mattress sutures are placed on the edges of the area of excision.
6. Subretinal fluid is released through a perforation made in the area of scleral excision.
7. A tube of polyethylene, 1.0 to 1.5 mm. in diameter, is placed under the sutures.
8. The sutures are drawn and tied over the polyethylene tubing.
9. A connection is made, with surface diathermy, between each end of the buckle and the ora serrata.

The advantages of the method may be summarized as follows:

The treated area is pushed toward the retina as much as evacuation of the subretinal fluid will permit; this insures closure of the retinal breaks at the time of surgery instead of later. It is unnecessary to give the patient preoperative bedrest as this might diminish the quantity of subretinal fluid available and would make the buckling operation difficult and less effective. Postoperatively, the bedrest period is limited to four to eight days; after this, no pinhole glasses are used. It is remarkable that if the same pre- and postoperative schedule is followed in cases of simple retinopexy, there will

still be failure in many cases.

The most important advantage of scleral buckling is that it is a very effective means of combating fixed retinal folds. The latter are the major obstacles to reattachment of the retina. The frequent occurrence of an equatorial fixed fold makes it necessary to place the buckle no further anterior than the equator. Because of its effectiveness against fixed retinal folds, scleral buckling makes it possible to reattach the retina in cases with an extremely poor prognosis.

In my hands, classical types of scleral resection have been much less effective, mainly because the ridge created in the walls of the eye is neither durable enough nor located properly in relation to the retinal breaks.

DR. CLARK: This I think is most interesting, but I should like to point out that there is an essential point of difference, in that the scleral shortening procedure to which I was referring was intended to create a simple detachment from a complicated one. It was based on the assumption that the present treatment of simple detachments was adequate.

I perhaps came to surgery of the eye through improper channels. I came in as a general surgeon and, therefore, I find it frightening, first, to contemplate the buckling operation and its creation of what we would term as a dead space and, second, to add a further complication to the dead space by implantation of a foreign body.

It is interesting to note that the full-thickness scleral buckle rejects the foreign body and resumes its normal shape (which demonstrates the tendency of all tissues to resume their normal positions) and yet the lamellar buckle is said not to. I would be interested if Dr. Schepens could tell us if there is any evidence of a return to its normal form when the buckle is done in the more usual area.

DR. SHAFER: I feel like a good little Republican at Truman's birthday party! Here I am surrounded by three ardent sclerectomists. Actually I am very much interested in Dr. Schepens' handling of the macular hole. There is a question coming up on it later, and I would like to add something to it. More directly, I wonder what is the fate of this retina that has been abandoned. What happens to the retina which is anterior to this buckle?

DR. SHIPMAN: I would like to ask Dr. Schepens what happens to the vortex veins when he is doing this procedure well back of the equator? If he is doing a sclerectomy—and from what I observed from his pictures he is doing a laminated sclerectomy as most of us do it and putting a polyethylene tube in the bottom part of it besides, which gives a nice buckle—I feel it would be a little safer to use some Walker pins back there rather than a resection with these tubes. You all know the vortex veins come in from five to nine mm. back of the equator, and there are four and sometimes five of them, and in taking out a piece of sclera four-mm. wide and 30-mm. long you are bound to encounter some of them. If the diathermy tip is used to obtain coagulations without cutting the sclera, I think it would be more advantageous.

DR. SCHEPENS: Scleral buckling creates an abnormal shape of the globe which is designed to reattach the retina as rapidly as possible. Methods of buckling tested so far permit one to create a ridge in the fundus which will stay between one month and six months or more, depending on the technique used. It is possible that no method of scleral buckling designed so far causes a permanent ridge in the fundus. In practically all cases, the tube is slowly pushed outward by the intraocular pressure. It is not extruded from the tissues but remains imprisoned under the scleral sutures, and becomes surrounded by newly formed connective tissue. Extrusion has been observed in less than one percent of the cases operated upon and is the result of faulty technique. When the ridge flattens out, after several months, it is rarely followed by a relapse of the detachment. The latter only occurs in particularly unfavorable

cases and special techniques have been developed for creating a buckle lasting at least six months in such cases.

Sections made through human specimens after this procedure show that the reaction caused by the polyethylene and the suture material is very mild.

The retina which is not treated and is anterior to the buckle remains detached and this seems to cause no trouble to the patient.

It is true that, in many cases, the buckle is located either over a vortex vein or its ampulla. With a proper technique this procedure can be done safely. A subchoroidal or vitreous hemorrhage is generally caused by pricking or tearing a venous channel and this we try to avoid carefully. When necessary one or even two vortex veins may be safely tied.

DR. MCLEAN: *Dr. Shafer, what are the rationale and indications for the use of vitreous in retinal detachment?*

DR. SHAFER: First, I want to explain what we are using as vitreous. This material, which is sterile pooled human vitreous, is extracted through an 18-gauge needle from eyes coming into the Eye-Bank for corneal transplantation. I have called the operation a vitreous implant. This is not to be confused with vitreous transplant which is done in cases of hemorrhage. In implant, we do not remove any vitreous; we are adding vitreous—so we implant vitreous.

The basic factors which make up the rationale for the use of vitreous are, I think, three:

The first I would call the anatomic factor. Anatomically we know that the retina is attached firmly at the disc and firmly at the ora. In between it is attached only by the very nebulous processes of the pigment cells; here is a loosely attached structure suspended across this arc of the choroid and sclera. The hypothesis was, and is, that the vitreous is an essentially normal support to the retina between its two strong attachments. By the same reasoning it would seem logical to implant vitreous to help reattach a retina that is detached and to keep the reattached retina attached. Clinically we know—for example, in cataract extraction—that the incidence of subsequent retinal detachment parallels the loss of vitreous.

Since the subretinal fluid is probably degenerated vitreous, this factor probably operates in most or all retinal detachments; therefore, there is a decrease in the normal vitreous volume. It would logically follow that implantation of more vitreous would represent more support to the retina.

The second factor for the rationale of vitreous implant I call the surge factor; it, of course, is not original with me. In following the movement of the eye, the vitreous continues to move and pull on any point where it is attached. It seems probable that many retinal detachments are preceded by the vitreous becoming detached posteriorly and coming forward. It would seem probable that this vitreous framework would be free to swing or pull on the remaining ora attachment in a low viscosity media, presumably intraocular fluid, posteriorly. It would therefore follow that implantation of more vitreous, a high viscosity medium, would tend to reduce the amount of surge and thus the amount of traction on the retina.

The third factor is purely surgical. By implanting vitreous, subretinal fluid is pushed out from behind the retina through the drainage hole; further the retina is pushed up against the choroid by the diathermy reaction.

To recapitulate, vitreous is implanted to supply more support for the retina, to reduce the surge factor, and to drive out the subretinal fluid, pushing the retina against the choroid.

Before showing slides illustrating the indications for vitreous implant in detachment of the retina, I want to say we have now done between 65 and 70 operations with vitreous, not all of them combined with retinal detachment. I want to emphasize that we have never lost an eye. There has been

no case of panophthalmitis or sympathetic ophthalmia. Postoperative vision has not been less than preoperative vision, even though the retina failed to reattach.

As for the indications, one of the men at the Manhattan Eye and Ear said that we operated on everything but cases of phthisis bulbi, and there was some doubt about that. In no instance was a fresh case involved in this series. They are all what Dr. Clark was talking about as belonging to Class 2 or 3. These are consecutive cases, and there was no selection.

The 42 consecutive cases of vitreous implant for retinal detachment included: three cases of Slaine implant plus diathermy failures; 12 cases of previous scleral resection, drainages or shortening failures; 14 cases with three or more previous diathermy or scleral surgery failures; 16 cases of aphakic detachments; eight previous failures with fixed folded retinas; 22 cases of total retinal detachments; eight cases with fixed vitreous bands. Most cases included one or more of the above characteristics.

Of these 42 cases which were all previous failures by an accepted technique 16 cases had aphakic detachment; 44 percent were reattached. Twenty-two cases had total detachment; 37 percent were reattached. Twenty-two cases had myopia of less than five diopters; 55 percent were reattached; four of them had five diopters or more of myopia, and 25 percent were reattached. Eight cases had fixed fibrous bands; 50 percent were reattached. Actually these results show the indications for vitreous implant.

The criterion of success for the over-all results is that all available retina be completely reattached for six months or longer. I say available retina because in this series are cases of retinal fibroplasia in which the periphery is no longer true retina, and we have reattached the posterior portion that remained as retina.

Of these 42 consecutive cases, all failures by previous methods, 48 percent were completely reattached by vitreous implant.

In summary, I want to thank Dr. Paton and Dr. Katzin for permitting me to work with the Eye-Bank and providing me with vitreous which made it possible to do two years of animal surgery before we dared try our first human case; and Dr. Milo Fritz, who is now practicing in Alaska, and who began to save vitreous, some of which is six and a half years old. To the best of my knowledge this was first done at the Eye-Bank. I also want to thank Dr. David Webster for his moral support and his technical support when things got difficult.

DR. MCLEAN: *Dr. Shipman, what are the relative merits of a lamellar resection versus a full-thickness scleral resection? What are the different indications for either of these?*

DR. SHIPMAN: I cannot refrain from congratulating Dr. Shafer on his excellent report of vitreous implants; his results are almost as good or better than I obtain in the usual run of cases. Certainly the results are as good or better than we get in resections.

Concerning the relative merits of the lamellar and complete resection, I do not do a complete resection any more. I think lamellar resection does everything that the complete does, and without the dangers. In the complete resection you are likely to lose subretinal fluid before you want to, and also, as Dr. Schepens has pointed out, all eyes have a tendency sooner or later to return to normal; the sutures either slough out or break, and the sclera comes back to the position it was in originally. If this happens in a complete resection (and I have seen it happen) you can get a marked herniation of the choroid, which is very embarrassing, to say the least. But with the lamellar resection you are much less likely to have this happen.

When a thin layer of sclera is left and it has been coagulated to a certain extent, a thin fibrous coating and a scar which is much firmer are more likely to result. For this reason I think the lamellar resection has definite advantages and the fluid can be let out

by different ways. Most of it I get out by pulling out the Walker pins. These pictures show that the tear has been localized; we go well back of this area and also surround the tear with Walker pins.

The tear has been localized by *direct* ophthalmoscopy and the point marked on the sclera. The area of the tear is completely surrounded and a barrage of coagulation is made in back of it. The area on the sclera to be resected is marked off; it is usually anterior to the tear. Scoring of this part is done with a Lundsgard's knife, tapering off at each end. The strip of sclera is then undermined with the Lundsgard's knife, and the outer four fifths of the sclera are completely removed. The piece of sclera to be resected is stripped off. I want to stress here a procedure which one of the residents at Wills Eye Hospital pointed out to me. I hope I am never too old to learn from a resident; at times, I think I learn from them more than they do from me.

The posterior edge of the sclera is undermined here and the anterior edge is undermined at the same level where we have cut down to the posterior layer, or one fifth of the sclera. Sutures are now placed. We use single-armed sutures, not a mattress suture for if it breaks you lose two sutures. Before the sutures are tied the loops are spread apart and this lower or deeper part of the resected area is coagulated with light diathermy, using the tip of the Walker electrode, with 20 to 30 ma. of current as recorded on our instrument, an Ophthalmotherme.

Continuing with lantern slides:

The Walker pins are pulled out here, as we are ready to tie our sutures. This lets the subretinal fluid gush out and helps the retina to float, or pop up rather suddenly, and come against the soft coagulum. Here is where the tear is, and we are anterior to it but we are definitely posterior to it here, and we must be. Dr. Schepens is right: you have to form a barrier back of the tear. Whether you create it with buckling or with coagulation of the sclera I think makes little difference, as long as you have shrunk the sclera enough to pull it with the choroid to the retina. You must have soft coagulum in the choroid back of the retinal tear so that when the structures come in contact an adhesion forms. These structures must be kept in contact long enough to insure a firm scar.

The next picture shows the rectus muscle reattached and the closing of the conjunctival wound with a continuous suture, which is very easy to remove one week later.

DR. MCLEAN: *Dr. Clark, what are the most important factors in employing diathermy on the eye?*

DR. CLARK: The most important factor is to know what you are doing.

The term "diathermy" refers to the heat produced by high frequency electrical currents encountering the resistance of tissues. In treating detachments we use this heat to produce the choroidal lesions whose adhesive reaction seals the retinal holes. However, all diathermy is not suitable for this purpose for the diathermy effect ranges from the pleasant warmth of the sinus-treating pad without damage to the most delicate cell to the instantaneous dissolution of tissue where the point of contact of the electrode resembles a knife cut.

The factors producing these differences are important and must be borne constantly in mind. In simplified form they are:

1. The heat produced is directly proportional to:
   a. The resistance encountered.
   b. The time of application.
   c. The square of the current.

Of these only the time is at the control of the surgeon, for the resistance of the tissues varies widely at each application of the electrode, and the current varies inversely with the area of the electrode contact.

2. The nature of the heating depends on the frequency and intensity of the current and on the pattern of the wavetrain, whether "damped" (irregular) as from a spark gap,

or "undamped" (uniform) as from a vacuum-tube oscillator.

a. The low-intensity, low-frequency damped current boils the tissue fluid and explodes the cells with their own steam. This is the "desiccating" or "fulgurating" current.

b. The high-intensity, low-frequency damped current produces dense coagulation and carbonization. This is the "coagulating" current.

c. The high-intensity, high-frequency undamped current produces dissolution of cells with little coagulation or carbonization. This current is called the "cutting" current.

d. The "blended" current is a combination of b and c.

3. The heating effect does not necessarily occur at the point of electrode contact but wherever a sufficient density of current meets sufficient resistance. We have specimens to show that this may be the bifurcation of a blood vessel as much as a centimeter from the point at which the electrode was applied. It follows, then, that the electrode employed should be as small as possible and applied as precisely as possible. The pointed electrode may be likened to the rifle; whereas the surface—ball electrode—resembles the shotgun.

4. Low-frequency currents are fickle and will always follow the path of least resistance. This may be the layer of moisture on the surface of the sclera, a blood vessel, the zonule of the lens, the vitreous.

The market of electrosurgical instruments is today flooded by a myriad of sleek, shiny instruments all labeled "diathermy" and all declared to be suitable for retinal detachment work. These instruments cover a frequency range from 50,000 to 27,000,000 cycles and wavetrain patterns of infinite variety and, added to this, tests show that the output of any two instruments of the same make differs widely in the spark-gap generator group. It is therefore important to know your own instrument.

DR. MCLEAN: *Dr. Schepens, what is your method of scleral depression? Are there any dangers involved in its use?*

DR. SCHEPENS: Scleral depression is more easily performed with an indirect stereoscopic ophthalmoscope, for the following reasons: The instrument has a better working distance and a stronger light than any direct ophthalmoscope; the field of view and depth of focus are considerably larger and this helps with orientation; stereopsis is also a considerable advantage.

For pressure on the sclera I use a small instrument mounted on a thimble and called a scleral depressor. It is very useful, although not indispensable, to dilate the pupil fully. When examining the upper or lower region of the fundus, pressure may be exerted over the eyelid; when the nasal or temporal portion of the fundus is to be examined pressure is exerted over the bulbar conjunctiva, after instillation of 0.5-percent tetracaine drops. Only very light pressure is required to see the ora serrata; the beginner generally presses too hard on the globe. If the intraocular pressure is markedly elevated, pressure is ineffective and should not be used; after intraocular surgery, scleral pressure should be deferred for six weeks.

No complications have been observed as a result of the correct use of scleral depression. This method appears as safe as tonometry or pupillary dilatation: such procedures may cause complications if the proper precautions are not taken but the information gathered by their use is useful enough so that it is reasonable to take this calculated risk.

DR. MCLEAN: *Dr. Shafer, how do you do a vitreous implant for detachment of the retina? Where do you get the vitreous?*

DR. SHAFER: Before we get into the diathermy part of the surgery, we prepare a sclerectomy, an incision at right angles to the limbus, about eight to 12 mm. behind the limbus, cut down through the sclera to the choroid and we put a mattress suture edge to edge through this incision and a second

mattress suture in the opposite direction so that there are opposing mattress sutures. We experimented with many different types of sutures and found that was the only one that would hold well at normal or higher-than-normal tension. Then the operator goes ahead with the normal diathermy technique, whatever that may be.

At the conclusion of diathermy and after provision for the subretinal drainage, a syringe filled with vitreous on a 18-gauge needle is put through the previously prepared sclerectomy, eight to nine mm. behind the limbus, after the choroid has been perforated by diathermy.

The assistant holds the pair of mattress sutures, the eye is brought up to whatever tension you wish—I have measured it at 70 on a tonometer, but normally I bring it to approximately 50, and hold it for two minutes —then the pressure of the eye is permitted to drop, as it does almost automatically from the subretinal fluid loss. The assistant pulls the sutures tight, the needle is withdrawn, there is usually maybe one drop of vitreous lost from the needle, and the sutures are tied.

One point that we have to be particularly careful about is striking the needle against the lens. In an aphakic eye there is, of course, no problem. We have tried the anterior route many times and found it much less successful.

Where do we get the vitreous? The vitreous comes from Eye-Bank eyes. This is sterile pooled human aspirated vitreous. The average eye will produce approximately two cc. of vitreous. It is obtained by piercing the seared sclera of the donor eye, about at the equator, and aspirating the vitreous with a sterile 18-gauge needle on a syringe. The vitreous is kept in a household refrigerator at 40°F. in rubber-capped glass vials.

DR. MCLEAN: *Dr. Shipman, under what circumstances do you advise against operation for retinal detachment?*

DR. SHIPMAN: When the patients do not want it, primarily. There are not many of these cases but, if the patient does not want operation, we will not operate. If the patient with only one eye wants an operation, that makes a difference. If diabetes with diabetic retinitis proliferans is present, that would influence us not to operate. I have always made it a practice to try to tell patients the truth, as far as I know it, in regard to what is going to happen if an operation is not performed; also how long hospitalization will be; how long they will be away from work, with a discussion of the expense of the entire procedure. After they know all the facts, if they still want to be operated on, I will do it.

DR. MCLEAN: *Dr. Clark, in re-operating on a case, how would you handle a sclera which has become partially necrotic from previous surface coagulation?*

DR. CLARK: Following either surface or penetrating diathermy, the sclera in the area of the treatment will not take sutures for three months. If a scleral shortening operation is deemed necessary, it must be done in another area. If vitreous traction is the causative force, the pole opposite the hole is usually the area of choice. If shrinkage or constricting membranes are the main cause of failure, the areas adjacent are usually best.

DR. MCLEAN: *Dr. Schepens, what is your technique for localizing tears during the operation?*

DR. SCHEPENS: For this purpose I use indirect stereoscopic ophthalmoscopy exclusively; some of the advantages of the method were described in my answer to "what is your method of scleral depression?" The small magnification obtained in indirect ophthalmoscopy helps to see through hazy media and in the extreme fundus periphery; the disadvantages of small magnification are offset by strong illumination.

For localization of a retinal break, the surgeon retracts the soft tissues from the globe in the quadrant under examination; the observer places the break in the middle of his

ophthalmoscopic field; this creates a red glow in the corresponding area of the sclera; the surgeon applies a flat diathermy electrode (which has an area of one square mm.) over the sclera, in the middle of the red glow; as the electrode is pressed firmly against the sclera, the observer sees a choroidal indentation and directs the surgeon as to exactly where the electrode should be applied; when the electrode is in the correct location, the diathermic current is released. A white mark will form in the retina only when the detachment is flat.

DR. MCLEAN: *Dr. Shafer, what is the importance of letting out fluid in retinal detachment surgery? What is your technique for this procedure?*

DR. SHAFER: I can see only one reason for letting the fluid out, and that is to permit the retina to go back against the choroid, or at least against the choroidal reaction.

As to the technique, I use one of two methods, depending on how far the retina is from the choroid. As Dr. Schepens and Dr. Clark mentioned, the great danger is in creating a new hole in the retina by the method you use to get out the fluid. Therefore if the retina is flat I usually make a tiny sclerotomy down to the choroid, until the choroid begins to herniate, and then open it with diathermy. Try and have the choroid bulge externally rather than having the tip of the electrode go in. If, however, the detachment is a large bullous one, I use pins with care that the tip of my pin does not touch the retina. The one advantage of pins is to save time.

DR. SCHEPENS: How do you know, when you use pins, that you are releasing the subretinal fluid; that it is not fluid vitreous escaping through new holes made in the retina by the pins?

DR. SHAFER: You can cause a tear, and you can certainly close it, when you see you have one with a pin.

DR. SCHEPENS: How do you know, when you operate on a case, that you are going to be successful? I have seen cases in which 10 or 15 additional retinal holes were caused by pins. If such a case is going to be successful, additional holes are unimportant; if it is not, they greatly complicate reoperation because such holes are always very small and difficult to detect.

DR. SHAFER: If we are dealing with a case in which the retina has flattened out, we do not put in pins; we use surface coagulation. I am talking about the big bullous detachments. I still feel that the Walker pin gives the best result with a resection in that type of case.

DR. CLARK: I just want to state there is one possibility by which both can be right, and that is by the injection of air, helium, argon, or vitreous. This definitely reduces the possibility of having a hole in the retina which is not in contact with the exudative area. We have found that closure by this exudate is complete within 36 hours, and any of these injected substances will hold the retina against the exudative area for that time.

DR. MCLEAN: *Dr. Shipman, how would you handle a detachment with a macular hole?*

DR. SHIPMAN: Personally I have not had too many to handle. It does not occur too often when a macular hole is alone, usually there are other holes. All of us, dozens of times, have seen so-called macular holes which never develop detachment, and it is very fortunate that they do not. I have always felt that most of these so-called holes are cysts. When a detachment does develop, I would treat it like any other type, except I do not use as much coagulation or current.

You cannot expect to get good results with these cases, and that is true in many detachments in which the macular area is involved. I always tell the patient in cases in which the age is over 50 years that they will never have reading vision when there has been a detachment of the retina in the macular area for over three days.

The three macular holes I have had the opportunity to treat I have treated with coagulation. Some men have advocated treatment with electrolysis or galvanic current, or using the undermining method with potassium hydroxide, as advocated by Lindner, but this is difficult to control. I have used this last method but not in macular holes. I would like to know what Dr. Schepens thinks.

DR. SCHEPENS: I completely agree with Dr. Shipman's statement that macular breaks are extremely rare; I found them present in about one percent of all cases of retinal detachment. In many instances, a macular break is mistakenly diagnosed and operated upon, when only a macular cyst is present. In a retinal detachment with peripheral breaks and where a macular break is suspected, I treat the peripheral breaks only. The suspected macular break is treated in a second operation, if this proves necessary.

DR. SHAFER: It is difficult to determine the macular breaks. With a borderline case, the peripheral tears are taken care of by diathermy and, if a detachment is not reattached, then we feel a macular tear should be assumed. In two cases, we used a thermophore at 160°F. for one minute, as described in the thermophore manual, with excellent results. The thermophore produces a very soft choroidal reaction, not as intense as one usually gets with diathermy.

DR. SHIPMAN: That was described by Langdon of Philadelphia about 15 years ago. I think he reported nine successful results out of 11 cases done by this method.

DR. MCLEAN: *Dr. Clark, what are the relative merits of the use of multiple pins versus a single electrode?*

DR. CLARK: The older, low-frequency, fickle currents require the use of micropins for penetrating application, for they allow multiple applications to be made without the escape of subretinal fluid which would dissipate the current. They also keep the globe firm which allows the force necessary to penetrate the sclera with these currents. Another point is the ease with which they can be visualized within the globe which insures the proper location of the treatment ring. They also leave a patent drainage hole for the subretinal fluid which the dense coagulum would otherwise plug.

Their disadvantages lie in their usual length which, with the current density greatest at the smallest diameter or tip, passes the choroid, where the reaction is desired, and may damage the retina. Further, the sudden removal of multiple pins is accompanied by a rush of fluid which sucks the retina into folds and does not allow it to settle smoothly.

With the more modern current the coagulum formed is not sufficient to hold the pins in place and they will drop out when they are released.

These higher frequency currents are not bothered by surface fluid so the single 0.5-mm. electrode is best, allowing adequate and widespread, slow, prolonged drainage and not endangering the retina.

DR. SHIPMAN: In line with the spurt you mentioned, don't you feel when you get 10 to 15 points squirting at once that you are going to get a vacuum which is more likely to encourage the retina to go to the coagulated areas in the choroid?

DR. CLARK: I think that you might better say jerk the retina in place.

DR. SHAFER: With the technique we use we do not have to worry about "jerking" or "squirting" because the subretinal fluid can be driven out according to the amount of vitreous we put in.

DR. SHIPMAN: You push it out with pressure from within.

DR. SCHEPENS: There is one disadvantage common to all methods of injection into the vitreous cavity. The size of the needle used for the injection is necessarily such that episcleral tissue will later grow into the vitreous, through the opening made in the sclera by the needle. Months or years later, this connective-tissue ingrowth may cause an incurable type of retinal detachment.

DR. MCLEAN: *How does your biomicroscopic examination of the vitreous influence your treatment of a case, Dr. Schepens?*

DR. SCHEPENS: In the majority of cases, biomicroscopic examination of the vitreous does not influence my surgical procedure. This examination only helps to explain certain features of a retinal detachment. For instance, fixed retinal folds are sometimes caused by traction bands or membranes in the vitreous, which cannot be seen by any other means of investigation. It is true that there are cases with fixed retinal folds which show no visible band or membrane in the vitreous cavity.

DR. SHIPMAN: Then you give a patient a poor prognosis when you find such folds?

DR. SCHEPENS: Yes.

DR. MCLEAN: *Dr. Shafer, what criteria do you use to determine that reoperation is necessary and how soon after an unsuccessful operation do you reoperate?*

DR. SHAFER: If, following surgery, I find: First, a new tear that was not incorporated in my diathermy and the retina is detached, it is obvious I have to reoperate. Second, if the retina is detached and the choroidal reaction is very thin, it is a failure and must be reoperated. In borderline cases where there is a small detachment in the periphery which has been surrounded by diathermy, the tear included within it, but the field starts to change, there is obviously a leak and that means reoperation. To me an important factor is the status of the other eye. If the other eye is blind then there is no choice about what you must do in a case of detachment. If, however, the patient has had four diathermies and two or three other assorted procedures and has spent most of the last year in the hospital, and so on, then sometimes we do not reoperate if the other eye is serviceable. I think, as Dr. Shipman said, a tremendous amount depends on the patient's decision as to whether they want you to reoperate.

When to operate I believe depends on an evaluation of the patient's general condition versus the status of the macula in the eye. If the patient is debilitated from continued surgery and the macula is not threatened, we may be able to postpone operation until the patient has been built up generally. If, however, the patient is in good condition and the macula is threatened, then we operate as soon as we can.

DR. MCLEAN: *What is your preoperative management of cases of retinal detachment, Dr. Shipman?*

DR. SHIPMAN: First we have to make the diagnosis of detachment—find the tear if we can; we cannot always find it. Certainly we have found it lately more than we used to. After we have found the tear, we tell the patient the whole story: what they are up against; what we think should be done, and we tell them that surgery is the only thing for their particular condition. If the patient agrees, we send them to the hospital and put them in bed in a position which will encourage gravity to help the detachment to settle back in place. I think I keep my patients longer in the hospital than some of the others here. I order pinhole goggles with three-mm. openings to be worn during the day. The pupil is kept dilated with atropine or, if necessary, some other mydriatics, and the eye is studied frequently ophthalmoscopically to see what is taking place, and look for the folds Dr. Schepens is talking about—not satisfied with finding one tear but looking for others.

The patient is prepared for general anesthesia. Formerly, two-percent novocaine was used retrobulbarly but I have been criticized for that. Now detachment cases are practically always done under intravenous sodium pentothal and the patient is kept in bed in a favorable position for five days. If the detachment shows no signs of going back, we operate, usually a resection. If the retina goes back, we are happy and feel there is a better chance for a successful result. These cases require a less formidable procedure.

DR. CLARK: Our preoperative regime is

based on three concepts:

1. A patient cannot be physically quiet unless he is mentally quiet.

2. A patient cannot be physically quiet unless he is comfortable.

3. The high-speed movements of the eye are the cause of the elevation of the retina and can best be stopped by firm, opaque bandages.

We, therefore, first give the patient a 12-hour period of bedrest without any eye cover (usually over the first night) so that he may get used to his surroundings and become familiar with the people who will care for him and see the manner in which things are done. During this time, every step of the procedure through his convalescence is explained in detail.

After this the eyes are bandaged and the patient is asked to lie quietly, with a Gatch bed to 30 degrees and slow turning of the head allowed. After 24 hours, the eyes are again examined and the bandages reapplied. Prior to the operation a final examination is done.

We have not found that the patient's position in relation to the position of the retinal elevation has any bearing on the speed of settling.

DR. SCHEPENS: After admission to the hospital, a complete examination of both eyes is performed; this includes visual fields, tonometry, slitlamp examination, and thorough fundus examination with the indirect stereoscopic ophthalmoscope. A detailed fundus sketch is made and checked by at least one other observer. A medical checkup is also performed and it always includes a chest X-ray study. The patient is neither given pinhole glasses nor put to bed, except when there is immediate danger of macular detachment. No preoperative flattening of the detachment is desirable before a buckling procedure. The morning of the operation, the patient is made to walk until he receives his preoperative sedation.

DR. SHAFER: I put my patients to bed with pinholes until I am convinced that we have the whole story from studies of the fundus. I think an important thing in the preoperative period is the other eye. Look at it, too. For dilatation I prefer five- to 10-percent homatropine and 10-percent neosynephrine, three times a day. The remaining regime is essentially what has been described.

DR. MCLEAN: *Dr. Shipman, what is your schedule for postoperative management in the hospital and after the patient is discharged from the hospital?*

DR. SHIPMAN: I do not dress the patient for 48 hours after surgery; dressing and atropine instillation are done daily after that. Patients are kept in the same position they were in before surgery. At the end of a week, I take the conjunctival sutures out. At the end of two weeks, I give the patients the same pinhole goggles they had before operation but still keep them in the same position; at the end of three weeks I start to get them up. I do this very gradually. I have had the experience of seeing more hemorrhages from getting patients up too fast, rather than from giving them too much diathermy current.

The day before the patient leaves the hospital I give him a six-mm. opening in the goggles and within two weeks, 12-mm. openings; in a month, 24-mm. openings. After another two to three weeks, a modified type of goggle is given. With these the patient can look at television and do a few things around the house. We gradually remove the black enamel from the back of these goggles, but still leave the temple guards on for another month. The patients usually do not want to take them off; they really get to like them. We feel that, after six months these patients are safe, and we then allow them to follow their usual routine and line of work; however, we have them report to the office every three months for a year and then check them every six months for a year or so, and then every year as long as they will come. How one can take a chance in these cases I cannot understand. I have never had

a patient object to waiting another month or two to get back to work, if he is getting a good result. I am happy, and so is the patient, and I think it is worth the effort.

DR. SCHEPENS: The postoperative management after scleral buckling differs from that following retinopexy. At the end of a scleral buckling operation, 200,000 units of penicillin, dissolved in one cc. of water, are injected into the orbit. Mydriatic drops are instilled and a pressure dressing is applied for 24-hours in order to avoid excessive swelling of the soft tissues. The dressing is renewed daily and a fundus examination is performed every day. In favorable cases the patient is given dark glasses and gets out of bed in four to six days; he is discharged from the hospital eight to 12 days after operation, and is kept on mydriatics for two more weeks; he is then allowed to return to work gradually.

More caution should be exercised in mobilizing a patient after retinopexy; it is generally not safe to let him out of bed for about 12 to 14 days.

DR. SHAFER: Postoperatively we do not do the first dressing for four days; then dressings are at four-to-five-day intervals until the 14th to 18th day, or whenever the choroidal reaction has ceased, at which time, if the operation is successful, the patients are given pinholes and permitted up by the 21st day. They are kept in pinholes for approximately another month, enlarging the pinholes as Dr. Shipman described. Pinholes are of tremendous psychologic advantage to a patient; in walking on the street he is not pushed around—the black glasses are as good as a warning to other people. I think they keep some retinas attached.

DR. CLARK: Our present schedule of postoperative care differs rather radically from those more generally followed. It arose from the careful analysis as to what were the essentials in many hundreds of cases. It has been gratifying to find that, in the three years and over 300 cases in which this schedule has been tried, our percentage of successes has risen and our percentage of recurrences decreased.

In essence we believe:

1. That the success or failure of the treatment has been determined when the patient leaves the operating table.

2. That the chief force affecting the separation of the retina is the inertia of the vitreous in the movements of the eye.

3. That the patient who rests in a comfortable position and moves slowly will be quieter than one who is tortured by forced immobility in an uncomfortable position.

The resulting schedule is:

1. At the end of surgery both eyes are bandaged and a protective mask applied.

2. Until he has reacted from his anesthetic, the patient is placed on the side which will allow the air bubble (injected into the vitreous space) to ride against the area of diathermy treatments.

3. After recovery from anesthesia, the patient is allowed to lie quietly as he chooses and have a Gatchbed up to 40 degrees. He is instructed again in slow movements but encouraged to exercise in this type of movements.

4. On the second postoperative day, the dressings are changed and the patient is allowed to be up in a chair as desired and allowed lavatory privileges. He may be shaved, brush his teeth, and comb his hair.

5. On the sixth day the dressings are changed for five-mm. pinhole goggles and the patient is allowed to walk about.

6. He is allowed home on the 10th to the 14th day. He is instructed simply to lead a quiet convalescent life with the avoidance of anything causing him to strain. He wears his pinhole glasses all the time his eyes are open but sleeps without a mask. Atropine (one percent) is instilled in the operated eye daily.

7. He is examined every two weeks and the pinhole glasses are removed at the end of a month.

8. During the second month, he gradually increases his activity to reach his normal

routine by the end of the month.

9. The final examination is done at the end of three months, and check-up examinations are done thereafter at six-month intervals. Both eyes are dilated to maximum at all examinations.

Not only has this regime improved our surgical results but the physical and mental status of our postoperative patients has improved so as to make the whole change seem worthwhile from that aspect alone.

DR. SHIPMAN: You are not allowing the patient to help cure himself. I also feel there usually is a certain amount of subretinal fluid left in the eye. I do not think we have to get it all out at the time of surgery; some of it will gradually seep out, and by the patient lying in bed in a position which will help it to settle, in two weeks the retina usually will be flat, even though it was elevated for a week or more after surgery. I would not get the patient out of bed under three weeks' time when the retina is still elevated. Perhaps all retinas in your cases are flat, Dr. Clark.

DR. CLARK: If you inject air you will have a flattened retina at the end of your operation. My only reply to the charge that the patients will not do so well is—that they seem to.

DR. SCHEPENS: There is one postoperative complication which was not mentioned, namely death following a circulatory accident caused by bedrest. Therefore, anything that can be done to shorten the bedrest period is of extreme importance.

DR. SHIPMAN: We have had well over 600 cases that have laid in bed for three weeks or longer, and we have yet to have a death. There has been one case of pneumonia, and I think that is a good record. More patients have died from getting up too soon. I have had them die after cataract operation getting out of bed, but I have not had them die in bed. I do not think the bad thing is the physical side; it is the financial loss to the patient and a gain to the hospital. Beds today are very scarce but I do not feel this should influence the handling of these cases.

DR. SCHEPENS: Out of nearly 3,000 operations for retinal detachment, performed since 1947, we have recorded five deaths resulting from pulmonary infarction; in each case it was felt that prolonged bedrest was a very important etiologic factor. Residents in other eye departments have reported to me 12 additional instances of death from this cause.

DR. SHIPMAN: We have internists observe and follow our cases quite carefully.

Jesse M. Levitt,
Recording Secretary.

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OCULAR OCHRONOSIS*

In 1948, Anderson† first reported a new ocular syndrome in industrial workers engaged in the manufacture of hydroquinone. Miller‡ has described in detail a small group of cases in this country. In this syndrome the cornea and conjunctiva are stained in the area of the palpebral fissure. The cornea has a brown sepialike stain which traverses the whole thickness of its substance and in severe cases may seriously impede vision. There are other changes which interfere with accurate vision—namely, vertical folds in

* Reprinted by permission from *The Lancet,* June 4, 1955.

† Anderson, B.: Arch. Ophth., **38**:312, 1948.

‡ Miller, S. J. H.: Tr. Ophth. Soc. U. Kingdom, **74**:349, 1954.

Descemet's membrane, a white precipitate within the corneal substance due to protein denaturation, deformation of the anterior surface of the cornea producing irregular astigmation, and in some cases ulceration. In the early stages the conjunctival changes consist in drying and thickening in the palpebral fissure, and this area later becomes yellow. Finally discrete dark patches develop over the white of the eye in the palpebral fissure on either side of the cornea, separated from it by a clear area. Once the corneal staining has appeared, there is likely to be permanent visual disability; this is not alleviated by contact lenses, but might conceivably be reduced by corneal grafting. The conjunctival staining gradually disappears without ill effect.

There seems little doubt that the main cause of this syndrome is lengthy exposure to the vapor and dust of quinone—an intermediate product in the manufacture of hydroquinone. Where the eye is protected by goggles or where the process is enclosed, the ocular changes do not arise. There is some slight evidence that long-continued exposure to an atmosphere heavily polluted with hydroquinone dust may produce corneal ulceration if the worker is unhygienic and careless in his protective habits; but some men have worked for 20 years in such an atmosphere without any change appearing. As far as is known, there has never been an instance of this syndrome in workers who handle hydroquinone during photographic development.

The clinical picture of this syndrome is of theoretical interest because it is almost identical with that of alkaptonuria and carbolic poisoning. The etiologic link is the staining of the eye either exogenously or endogenously by a salt of hydroquinone. For this reason the three conditions have been grouped together under the name ochronosis —a word coined by Virchow,[1] who first described the pathologic findings in alkaptonuria and wished to distinguish the disorder from melanosis.

[1] Virchow, R.: Virchow's Arch., **37**:212, 1866.

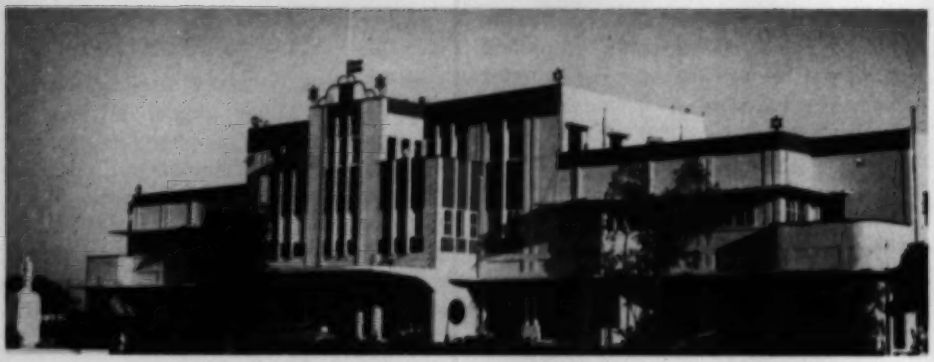
ALIGARH MUSLIM UNIVERSITY INSTITUTE OF OPHTHALMOLOGY

At a brilliant ceremony, presided over by Shri Chandra Bhan Gupta, Minister of Health, Government of Ultar Pradesh, and attended by more than 2,000 dignitaries, ministers of the Union, and officials of the state governments, Sri Jawahar Lal Nehru, Prime Minister of India, officially opened the Muslim University Institute of Ophthalmology at Aligarh, India, on November 12, 1955. The occasion also marked the Silver Jubilee of the Gandhi Eye Hospital.

The Aligarh Muslim University Institute of Ophthalmology, whose cornerstone was laid by Rajkumari Amrit Kaur, Minister of Health, Government of India, on January 3, 1952, was established to develop a center for advanced education and research in ophthalmology. Housed in a beautifully designed modern building, it is operated in close collaboration with the Gandhi Eye hospital which has been serving a great need for over a quarter of a century.

That the Aligarh Muslim University Institute of Ophthalmology is dedicated to advancing ophthalmic research and education

Prime Minister of India Nehru at the opening ceremonies



The Aligarh Muslim University Institute of Ophthalmology

shows the determination of Indian ophthalmology to develop its medical organization and to work shoulder to shoulder with similar institutions all over the world, but particularly those of the West, in the advancement of our science.

India has a wealth of clinical material; this very abundance has hindered scientific development—for the need of patients has had to come first and doctors have had little time or energy left to devote to pure science. This new institute is fortunate in that it has been able to recruit a staff of enthusiastic research workers who are exempt from routine clinical work, whose duties are to develop postgraduate ophthalmic education and to advance ophthalmic knowledge in the institute's elaborate laboratories.

THE JOURNAL extends its congratulations to the Aligarh Institute of Ophthalmology and asks for the Blessing of this great new eye institute in India. Its establishment is a wonderful thing for world ophthalmology and all of us await with interest its contributions to our knowledge.

Derrick Vail.

OBITUARIES

JAMES W. SMITH
(1893-1955)

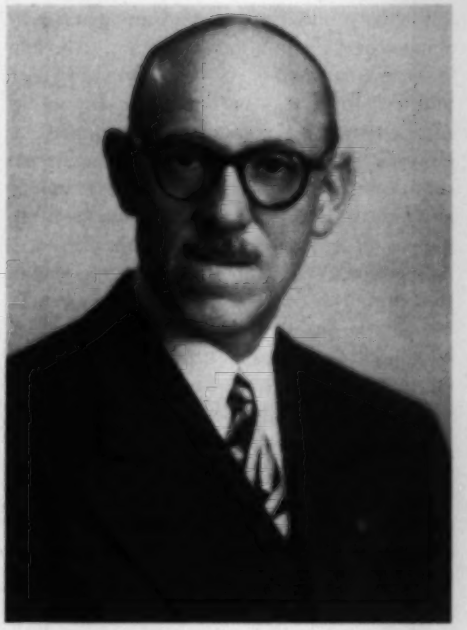
James W. Smith will be long remembered by his many friends and colleagues everywhere as an inspiring teacher and a wise leader and counsellor.

It was his love for teaching which accounted for the perennial popularity of—to cite but one example—his course on "Practical points in office treatment" which used to draw capacity audiences at the annual meetings of the American Academy of Ophthalmology and Otolaryngology.

The chief beneficiaries of Jim Smith's leadership and advice were the members and officers of the New York Society for Clinical Ophthalmology which he helped found more than 20 years ago and which, in 1941, elected him president. Year after year, Jim could be counted upon to act as toastmaster at the society's annual dinners where he would amaze and awe his audience by the display of his phenomenal memory for both faces and names.

James W. Smith was born in Washington, D.C., May 16, 1893. He received his medical degree from the New York University College of Medicine in 1917. During War I (1918-19) he served as first lieutenant in the Medical Corps of the U.S. Army.

In 1919, he began the private practice of ophthalmology and joined the staff of the Post-Graduate Hospital. When the latter became affiliated with New York University a few years ago, Jim was made attending ophthalmologist and clinical professor of ophthalmology at the New York University



JAMES W. SMITH

Bellevue Medical Center. He was also chief of the Eye Service of the Hospital for Joint Diseases and Consulting Ophthalmologist of Goldwater Hospital.

Jim Smith displayed his talent for leadership in every group which he joined. A Life Fellow of the New York Academy of Medicine, he was chosen as chairman of its Eye Section for 1951-52. His election as president of the Alumni Association of the New York University College of Medicine for 1939-40 was a fitting reward for his many years' activity in, and devotion to, this organization. Similarly, his many years of activity in the Phi Delta Epsilon Fraternity culminated in his election as president of the board of trustees for 1950-51.

He contributed over 40 papers to the ophthalmic literature. Several of his papers dealt with strabismus, a subject in which he became interested through his close association with James W. White. Yet, his interests were so diversified that they embraced the entire field of ophthalmology. Jim was always practical and down-to-earth. He tried to convey the same attitude to his listening and reading audiences. Among his papers may be mentioned: "Spontaneous dislocation of the lacrimal glands"; "Senile hyaline scleral plaques"; "Ochronosis of sclera and cornea complicating alkaptonuria"; "Problem of strabismus in childhood"; and "Strabismus in young infants."

As much time as Jim could snatch from his professional pursuits he devoted to a most interesting hobby: the collection of old historical letters and manuscripts. His large collection of letters by American presidents dealt chiefly with medical subjects. He cherished especially those letters which had ophthalmologic interest. Several of these bits of Americana were published from time to time in THE JOURNAL as "Ophthalmic Miniatures." This hobby led him to become one of the founders of the Manuscript Society which in 1948 was reorganized as the National Society of Autograph Collectors.

James W. Smith died on October 24, 1955, after a short illness. He is survived by his widow, Sarah Pollock Smith, and their son, Dr. Barry F. Smith.

Adolph Posner.

THOMAS DYER ALLEN
(1888-1956)

Dr. Thomas Dyer Allen was born in Omaha, Nebraska, on April 18, 1888. He was the son of Dr. Edmund T. Allen, who was an ophthalmologist and otolaryngologist, and Dr. Abbie Dyer Allen.

His family was not wealthy and there were many moves during his childhood, but Tom Allen was graduated from the University of Wisconsin in 1913 and from Rush Medical School in 1915.

He interned at St. Luke's Hospital in Chicago and became associated with Dr. William H. Wilder in the private practice of ophthalmology.

There was no question that Tom Allen was to become an ophthalmologist. As a youth, he

THOMAS DYER ALLEN

received instruction from his father in optics and he earned his way through school fitting and selling glasses or working in the optical business. These experiences made a deep impression on him, and, in his later years, he referred to them again and again; and always one of his favorite teaching subjects was refraction.

Tom Allen had several characteristics which set him apart from ordinary people. He had a tremendous intellectual curiosity and a great drive to satisfy this curiosity. This was a characteristic of all the Allens; education was extremely important, and nothing was to stand in the way of achieving this education.

Those who came in casual contact with him were most impressed by his enthusiasm. He had a way of verbalizing this enthusiasm that was all his own, starting off with a "By golly!" or a "By thunder!" with a rising inflection of his voice.

I never heard him make a prejudiced remark. He accepted people for what they were and did his best to help everyone. He was very generous, and at times, I suspect, his enthusiasm may have colored this generosity somewhat.

Tom Allen had a strong social conscience and felt that it was important for every physician to be a responsible member of society. Several of his major interests reflected this feeling strongly. He was the secretary general for North of Panama of the Pan-American Association of Ophthalmology and he gave of himself unstintingly in service to this organization. He was largely responsible for the growth of the association which has become a real force in the whole field of ophthalmology. He was an active and interested member of the Illinois Society for the Prevention of Blindness. He was interested and played an important role in the education of young ophthalmologists and a whole generation recalls the vigor and enthusiasm of his teaching. He was an associate professor of ophthalmology at the University of Illinois.

He was a member and past president of the Chicago Ophthalmological Society; a member of the American Ophthalmological Society; a member and past councillor of the American Academy of Ophthalmology and Otolaryngology; a member of The Institute of Medicine of Chicago; and of the American Medical Association.

Thomas Dyer Allen died February 14, 1956, after a long illness. He is survived by his widow, Ruth Delzell Allen, six children and 13 grandchildren.

Daniel Snydacker.

CORRESPONDENCE

EYE AND HAND

Editor,
American Journal of Ophthalmology:

Recently there consulted me a man who was no longer able to work because he could not manage his tools. He was a carpenter who, a year or so ago, was wounded in his left eye, scarring the cornea and the iris, the lens becoming opaque. He was an expert workman, having assigned to him the joining

of the trim and other fine pieces. He cannot strike the nails and otherwise carry on. He had been aware of the difference in the skill of the two eyes.

This man is approximately 60 years of age, has worn bifocal spectacles which, at present, brought his vision to 6/18. He has not been granted work because of his disability. As his work has always required that he employ both right and left hands, he had regarded himself as "equal handed."

The recording of this case revived in my thoughts of earlier times a consideration of the powers of the eyes and hands, one with the other, that is whether one is right-eyed and right-handed, or left-eyed and left-handed, or cross-handed and opposed-eyed, the eyes are in all other respects healthy and normal.

In the studies of young children and other youthful persons both eyedness and handedness have been considered as a whole. It had been the habit since remote times to attend only to the use of the hands. Left-handedness has been a "shameful" fault and yet, in efforts to correct an individual, compelling the use of the right hand, serious nervous symptoms are likely to develop in a sensitive child who endeavors to train his right hand to the degree of usefulness natural in his left hand. He stutters and blinks his eyes, while the hand might tremble and never equal the natural skill for his purposes. In such cases a testing of the sight might reveal that powers of the two eyes exhibit a dominance of the left eye—thus accompanying the left handedness. In observing very young children, eye dominance may correspond to the hand naturally exercised. In other words, crossed actions are rarely, if ever, natural; among those who have acquired crossed manifestations have been found those who are backward in their studies and clumsy in their play. Seldom, indeed, if ever, does one find right-eyedness in a left-handed person.

The sight and handedness may be found somewhat as follows: (1) equality of the two eyes and action of the two hands; (2) dominance of the right eye and right hand; (3) dominance of the left eye and left hand; (4) mixed eyedness and handedness—right or left.

Outline for a scheme for study of "ocular dominance"

I. For the purpose of study certain classifications might be considered, first obtaining a history of handedness. Those with left eye might have been left handed. Those using right hand might have been left naturally but have acquired the use of the right hand. In no case should a difference in refractive measures be included in the study of any subject manifesting individual dominance:

1. Pupils, aged 8 to 14 years, backward at school. Evidences of eye dominance and handedness—right or left. Right eye and right hand; left eye and right hand.

2. Those aged 10 to 14 years, of more than average advancement in school work. Right eye and right hand; left eye and right hand.

3. A group of all ages, including masters—adults, but known to have imperfect sight, as requiring glasses, including the strabismic. Right eye and right hand. Left eye and left hand. Complete sidedness. Left eye and right hand.

II. Tests for the recognition of the dominant eye.

1. *Sighting.* A rough test to give an indication of which eye is dominant. Point with finger at a small distant object, such as a candle light; each eye alternately occluded, the dominant is that with which the finger is in alignment.

2. *Peep hole.* Card with 0.75-inch diameter hole in the center. (a) Subject holding card at arm's length suddenly swings it up before his face, looks through the hole at spotlight. Alternate occlusion. Dominant is the one used to see the light. This test is accurate if the subject does not deliberately select the eye with which he looks through the hole. The test should be repeated several times to insure accuracy. (b) Object held before face of subject who looks at it through the hole as

observer notes which eye is used. This test is useful for children and to confirm (a).

3. *Alignment.* Subject holding pencil or short rod vertically in front of him about one meter distant tells investigator how to move object to bring it in line with the spotlight. Physiologic diplopia occurring may not be observed by the subject. The more marked the dominance the less he notices the second image. If he does, he is instructed to set the clearer image in line with the light. The clearer image belongs to the master eye. Each eye occluded alternately, the dominant is that seeing the pencil or rod still in alignment, handedness of the subject being eliminated.

4. *Cone test.* Three small cones are placed on a table a meter distant, separated from one another about six inches. With the large surface of a cone held before the face, its point directed to the central object, subject stating whether the right or left is the distant one.

5. *Near-point convergence test.* Dominant is the one that fixes, the other diverges.

Marked degrees have been found among those manifesting crossed dominance. Maddox-rod tests might elicit inequalities in the sizes of the images. Also, it must be borne in mind that a degree of aniseikonia might be present and effect the individual's perception.

Observation might be carried out by noting to which side a book might be held while reading, as in marked cases the page is held towards the side of the dominant eye. In them, the size of the images of the two eyes are likely to vary.

As might be expected in the observation by experienced persons in strabismic persons the straight eye is the dominant.

One must attend to statements by parents the child might have manifested early a left-handedness which state was considered as a bad habit and every effort had been made to "correct the habit" with the consequent development of a crossed ocular dominance. The wise parent is one who allows the native dominance to be maintained yet, without painful insistence, encourages direction of the development of accuracy in the skill of the nondominant hand. In later years occupation and technique might require the equal usefulness of the two hands; watchmakers, certain handicrafts and indeed even operative surgery might demand an almost equality of action, demanding co-ordination of eye and hand.

In the refraction and subsequent prescription for glasses, it is of extreme importance that the state of dominance should be taken into account. The dominant eye must be given the preference. This is to be especially noted in anisometropia, and the dominant eye is to be given the better vision. Care must be taken that the dominant eye shall not have the magnified image. In cases of myopia in which full acuteness has been obtained, it is necessary for the maintenance of comfortable sight that equality should be sought for. Monocular myopia might express dominance of the normal eye, but the correction of the myopia and the prescription speedily balances the images of the two eyes and enables the wearer to be free from asthenopia.

Presbyopia correction should be so ordered that the near-point of the dominant eye shall not be farther away than that for the other eye.

Pronounced cases of inequality. The patient had been in the habit of holding his page before the dominant eye. The reading segments in such cases should be set before the nondominant eye a mm. or two nasalward, and that before the fellow a mm. or two to the temporal, thus allowing the axes to pass through the centers of the reading segments.

It is a fact that all sight is appreciated through cerebral comprehension; this is equally true of the dominance of one or other of the eyes.

(Signed) Burton Chance,
Philadelphia, Pennsylvania.

BOOK REVIEWS

THE PREVENTION OF DISEASE IN EVERYDAY PRACTICE. By Isadore Givner, M.D., F.A.C.S., and Maurice Bruger, M.D., F.A.C.P., and contributors. St. Louis, C. V. Mosby Co., 1955. 964 pages with 50 text illustrations and frontispiece in color, chapter bibliographies, index. Price: $20.00.

The message of this book is not the remarkable strides in preventive medicine accomplished by public health measures but rather the vast perspective in this field that exists in every doctor's private practice. The 47 contributors ably present the responsibilities that challenge every practitioner of medicine. To quote from them:

"Prevention is the most effective, indeed the only truly successful, procedure employed in clinical allergic problems."

"Certain circumstances that can be noted, foreseen and forestalled, invite, and practically at times, compel accidents."

"The ideal diabetic detection center is the office of the family physician."

"Maternal infections, particularly those of a viral nature, may lead in the offspring to congenital abnormalities, including malformations of the heart."

"Every physician, regardless of his specialty, has an important role to play in preventive psychiatry."

"Loss of teeth is not considered inevitable."

"Smoking is primarily responsible for the great increase in lung cancer."

"To detect symptomless glaucoma cases, we must educate the optometrists. Eye societies should arrange a list of willing lecturers to optometrists to keep the subject constantly in their minds."

"All of us can do much to prevent some eye disease if we utilize existing knowledge."

The many aspects of preventive ophthalmology are surveyed by Givner, including iatrogenic causes of visual loss, the retinopathy of prematurity, industrial ophthalmology, and genetic factors. Additional chapters by Byron Smith, Chandler, Schepens, and McLean consider the preventive implications in the interventions for plastic surgery, glaucoma, retinal detachment, and cataract, respectively.

The chapter on anesthesia emphasizes that "By depressing the vagus with adequate amounts of atropine, cardiac arrest can be prevented. The importance of the oculocardiac reflex, adequately presented by Walsh in his *Clinical Neuro-Ophthalmology*, is nowhere mentioned. In ophthalmic surgery under general anesthesia this may be a contributing factor to cardiac arrest if no retrobulbar injection is given and if systemic atropinization is inadequate, as often happens in muscle operations on children.

This is a book with a mission to which all disciples of Aesculapius should harken. The best preventative of the complications of disease is early, effective and thorough treatment.

James E. Lebensohn.

A TEXTBOOK OF MEDICINE. Edited by R. L. Cecil and R. F. Loeb. Philadelphia-London, W. B. Saunders Company, 1955, 9th edition. 1,786 pages, index. Price: $15.00.

This, by now, standard textbook of medicine has properly appeared in its ninth edition. The editors, Russell L. Cecil, professor of clinical medicine emeritus, Cornell, and Robert F. Loeb, Bard professor of medicine, Columbia University, together with their associate editors, Prof. A. B. Gutman of Columbia, Prof. W. McDermott of Cornell, and Prof. H. G. Wolff of Cornell, have been aided in this important task by 168 well-known authorities in medicine and surgery in the United States, as contributors.

Thirty-nine new subjects not covered in previous editions (last one 1951) have been added. This shows some of the rapid advances in Internal Medicine in the last few years.

There is much of interest to ophthalmologists in this new edition. The work is skillfully done and carefully edited. The illustrations are adequate and the printing excellent. It is highly recommended.

Derrick Vail.

STATIC AND DYNAMIC ELECTRON OPTICS. An account of focusing in lens, deflector and accelerator. Cambridge Monographs on Mechanics and Applied Mathematics. P. A. Sturrock. London, Cambridge University Press, 1955. 240 pages. Price: $5.50.

The ophthalmologist is familiar with electron optics almost wholly from the outstanding feats performed by the electron microscope in exploring and bringing to light minute structures which are beyond the resolution limits of the ordinary microscope. His interests have been in the results or possible applications, and not in the underlying theory of electron optics. Therefore, this book will hold no interest for ophthalmologists generally, although physicists associated with medical researchers will recognize it as a worthwhile contribution to the literature of electron optics.

Dr. Sturrock's treatment of the subject is purely from a theoretic standpoint, in which he presupposes the reader to be fully acquainted with matrix and vector mathematical techniques. It is a book for specialists who have long since lost the need (and possibily the capability) to think of electron optics in terms of parallels with "light" optics. The latter field is several centuries old and was cleverly developed on the basis of mechanistic models which enabled the nonspecialist to gain a practical understanding of applied optics without formal mathematical training beyond trigonometry. Electron optics is a new field, having begun in 1926 when the German physicist, H. Busch, showed that electron beams could be focused by magnetic and electric fields the same as lenses can focus a light beam. As a result, our knowledge of electron optics has developed from the efforts of theoretical physicists who could not care less if their computations made little sense to practitioners. Thus, there is hardly any hope that the ophthalmologist can ever gain a useful mental picture of electron optics in the same sense that he enjoys a familiarity with lens optics which he can visualize as models that function according to simple rules in spite of their rigorous and complicated mathematical formalities when treated according to Maxwellian and Hamiltonian electromagnetic wave concepts.

Lloyd E. Varden,
Associate Professor in Engineering,
Columbia University,
New York.

LE SYSTEME NERVEUX PERIPHERIQUE. By Guy Lazorthes, M.D. Paris, Masson et Cie, 1955. 348 pages, 214 figures, index. Price: Clothbound, 4200 fr.; paperbound, 3500 fr.

The author, a professor of anatomy at Toulouse and a practicing neurosurgeon, integrates in this book—his third on the nervous system—the comprehensive details of the anatomy and physiology of the cranial and spinal nerves in relation to clinical disorders, methods of examination and surgical treatment. The text is complete but compact and illustrated profusely by figures that are models of simplicity and interpretation. Of special interest to the ophthalmologist are the several chapters devoted to the optic, ocular motor, trigeminal, and facial nerves.

James E. Lebensohn.

PROGRAM*

of the

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY

Oceanic Room—Hotel Knickerbocker—Chicago, Illinois

June 11 through June 14, 1956

Monday afternoon, June 11, 1956

REACTIONS OF THE ELEMENTS OF RETINA AND OPTIC NERVE IN COMMON MORBID ENTITIES OF THE HUMAN EYE
J. Reimer Wolter

OBSERVATIONS ON THE TREATMENT OF A RABBIT TUMOR TRANSPLANT INTO THE FUNDUS
Adolph W. Vogel

EXPERIMENTS ON WOUND HEALING IN THE ENDOTHELIUM OF THE CORNEA
Rudolf F. Binder and Hertha Binder

THE OCCURRENCE OF LENS CHANGES FOLLOWING IRRADIATION OF SINGLE AND MULTIPLE QUADRANTS
R. D. Richards, Edward Riley and P. J. Leinfelder

THE EFFECT OF MODERATE DOSES OF X-RAY IRRADIATION ON OCULAR TISSUES
Bernard Becker, Marguerite A. Constant, Paul A. Cibis, Michel Ter-Pogossian and Rosalie Smith

CLINICAL AND EXPERIMENTAL FUNGUS INFECTIONS OF THE CORNEA
Albert P. Ley

A STUDY OF STRAINS OF APC VIRUS ISOLATED FROM PATIENTS WITH KERATOCONJUNCTIVITIS
A. Fowle, V. Simmons and H. L. Ormsby

OBSERVATIONS ON EXPERIMENTAL TRACHOMA AND INCLUSION CONJUNCTIVITIS
T. T. Crocker and Phillips Thygeson

PERSISTENCE OF TOXOPLASMA EXPERIMENTALLY INOCULATED INTO GUINEA PIGS' EYES
Michael J. Hogan, Phyllis Zweigart and Ann Lewis

OCULAR PENETRATION OF ANTIBIOTICS BY IONTOPHORESIS
S. H. Witzel, I. Fielding and H. L. Ormsby

A COMPARATIVE STUDY OF SCLERAL SHORTENING OPERATIONS IN RABBITS
William G. Everett

Tuesday morning, June 12, 1956

THE ARGYLL ROBERTSON PUPILLARY SYNDROME
Otto Lowenstein

STUDIES ON THE AUTONOMIC INNERVATION OF THE IRIS
Julia T. Apter

SOME MECHANISMS OF CENTRALLY INDUCED EYE PRESSURE RESPONSES
Ludwig von Sallmann, Frank Macri, Theodor Wanko and Patricia Grimes

STUDY ON THE INNERVATION OF THE ANTERIOR CHAMBER ANGLE
Monte Holland, Ludwig von Sallmann and Eleanor Collins

THE TECHNIQUE OF DETERMINATION OF BLOOD VOLUME CHANGES IN THE CHOROID AND RETINA
J. W. Bettman and Victor G. Fellows

CATIONS AND THE CORNEAL STROMA
W. Morton Grant

MEASUREMENTS OF AQUEOUS OUTFLOW IN ENUCLEATED EYES
E. W. Purnell, C. E. Melton, Jr., and E. Q. Adams

SPECIES VARIATION IN FACILITY OF AQUEOUS OUTFLOW
Bernard Becker and Marguerite A. Constant

PHYSIOLOGIC VARIATIONS OF BICARBONATE ION CONCENTRATION IN THE INTRAOCULAR FLUIDS
Harry Green and Irving H. Leopold

Wednesday morning, June 13, 1956

SPECTRO-DIFFERENTIAL ELECTRORETINOGRAPHY IN MACULAR DISEASE
Jerry Hart Jacobson and Demir Basar

THE EFFECT OF HALLUCINOGENIC DRUGS ON THE ELECTRORETINOGRAM
Julia T. Apter

CLINICAL STUDIES WITH FLICKER ELECTRORETINOGRAPHY
Gilbert Iser and George Goodman

THE EFFECT OF RATE OF RISE OF PHOTIC STIMULI ON THE HUMAN ELECTRORETINOGRAM
Hans Bornschein and Ralph D. Gunkel

BUSINESS MEETING

STUDIES ON THE VISUAL TOXICITY OF METHANOL: IX. THE EFFECT OF ETHANOL AND METHANOL POISONING ON THE RHESUS MONKEY
Anita P. Gilger and Albert M. Potts

* Abstracts of the papers to be presented before the Association for Research will be published in the *Ophthalmic Research Department* in the May, 1956, issue of THE JOURNAL.

ROD AND CONE VISION IN RETINITIS PIGMENTOSA
Bernard H. Zeavin and George Wald

RESIDUAL PROTEINS OF THE VITREOUS
Anita Suran and W. K. McEwen

THE DEVELOPMENT OF ORBITAL FASCIA
Walter H. Fink

MICROSCOPY WITH A NEW ILLUMINATION TECHNIQUE
Paul A. Cibis

Thursday morning, June 14, 1956

A QUANTITATIVE ANALYSIS OF THE HORIZONTAL MOVEMENTS OF THE EYES IN THE EXPERIMENT OF JOHANNES MUELLER
Matthew Alpern

SOME PHYSIOLOGIC CONSIDERATIONS OF HEREDITARY MACULAR DEGENERATION
Rodney D. Steinmetz and Kenneth N. Ogle

EYE MOVEMENTS IN AN ADULT WITH CEREBRAL HEMISPHERECTOMY FOR TUMOR
David Volk and Jan H. Bruell

CORNEAL TRANSPORT OF LACTIC ACID AS MEASURED WITH C-14 LACTATE
Albert M. Potts and B. Cohen

THE HYDRATION OF THE CORNEA: II. THE INFLUENCE OF THE EPITHELIUM AND INTRAOCULAR PRESSURE
John E. Harris, Leta B. Gehrsitz and Louise Gruber

EFFECT OF CASTRATION ON GALACTOSE CATARACT
Robert A. Resnik and Eugene Streicher

ENZYMATIC ACTIVITIES OF LENS: A PRELIMINARY SURVEY
Bernard Wortman and Bernard Becker

EFFECT OF AGE UPON LENS METABOLISM
Harry Green, S. A. Solomon and Irving H. Leopold

ENZYME SYSTEMS CONCERNED WITH OXIDATIVE PHOSPHORYLATION IN CILIARY PROCESSES
Elmer J. Ballintine and Morton B. Waitzman

THE ENERGY REQUIREMENTS OF THE LENS: THE ABILITY OF VARIOUS METABOLITES TO REPLACE GLUCOSE AS SUBSTRATE
Daniel J. Heinrichs and John E. Harris

PROGRAM

of the

SECTION ON OPHTHALMOLOGY

American Medical Association

Oceanic Room—Hotel Knickerbocker—Chicago, Illinois

June 12 through June 14, 1956

Tuesday afternoon, June 12, 1956

CHAIRMAN'S ADDRESS: FOVEAL CO-ORDINATION: THE MAJOR FACTOR IN VISUAL LEARNING
A. D. Ruedemann, Sr., Detroit

ADDRESS OF GUEST OF HONOR: OCULAR FINDINGS ASSOCIATED WITH MENINGIOMAS OF THE TUBERCULUM SELLAE
(Guest of honor) Francis C. Grant and Thomas R. Hedges, Jr., Philadelphia

REPORT OF 500 PATIENTS EXAMINED FOR LOW VISION
Gerald Fonda, Short Hills, New Jersey
Discussion to be opened by: William F. Murrah, Memphis

UNILATERAL INTERNUCLEAR OPHTHALMOPLEGIA OF VASCULAR ORIGIN
Max Fine and Charles B. MacGlashan, Jr., San Francisco
Discussion to be opened by: Francis Heed Adler, Philadelphia

BULLOUS KERATOPATHY
A. Ray Irvine, Jr., Los Angeles
Discussion to be opened by: David G. Cogan, Boston

HAZARDS OF THE USE OF SYMPATHOMIMETIC DRUGS IN OPHTHALMOLOGY
William U. McReynolds, Quincy, Illinois, William H. Havener, Columbus, Ohio, and John W. Henderson, Ann Arbor, Michigan
Discussion to be opened by: Frederick H. Theodore, New York

BUSINESS MEETING

Wednesday afternoon, June 13, 1956

ELECTION OF OFFICERS

A NEW MAGNETIC ORBITAL IMPLANT
Orwyn H. Ellis and O. Robert Levy, Los Angeles
Discussion to be opened by: Richard C. Troutman, Brooklyn

HYPERSECRETION GLAUCOMA
Bernard Becker, G. R. Keskey, and R. E. Christensen, St. Louis
Discussion to be opened by: W. Morton Grant, Boston

OBSERVATIONS ON THE DISSIMILARITY BETWEEN THE RETINAL CAPILLARY MICROANEURYSM IN DIABETES MELLITUS AND THE NODULE OF INTERCAPILLARY GLOMERULOSCLEROSIS
David Volk, Cleveland
Discussion to be opened by: A. Edward Maumanee, Baltimore

PSEUDOSTRABISMUS CAUSED BY HETEROTROPIA MACULAE
Harry Horwich, Biloxi, Mississippi
Discussion to be opened by: Harold W. Brown, New York

INFLAMMATION OF THE RETINAL ARTERIOLES AND VEINS WITH OR WITHOUT ASSOCIATED INTRAOCULAR HEMORRHAGES (EALES' DISEASE)
Samuel J. Kimura, Michael J. Hogan, and Frederick R. Carriker, San Francisco
Discussion to be opened by: Georgiana Theobald, Oak Park, Illinois

A SURVEY OF THE PATHOGENESIS OF RETINAL OCCLUSION WITH EMPHASIS UPON CHOICE OF THERAPY, AND AN ANALYSIS OF THE THERAPEUTIC RESULTS IN 60 PATIENTS
Bertha A. Klien, Chicago
Discussion to be opened by: John McGavic, Bryn Mawr, Pennsylvania

Thursday afternoon, June 14, 1956

THE USE OF RETROBULBAR AIR AND LAMINOGRAPHY IN THE LOCALIZATION OF ORBITAL TUMORS
G. R. Keskey and W. R. Letsch, St. Louis
Discussion to be opened by: Ira S. Jones, New York

OBSERVATIONS ON HERPETIC KERATITIS
Phillips Thygeson and Samuel J. Kimura, San Francisco
Discussion to be opened by: Trygve Gundersen, Boston

FUNGUS KERATITIS
T. E. Sanders and Albert P. Ley, St. Louis
Discussion to be opened by: E. R. Veirs, Temple, Texas

VERTICAL MUSCLE IMBALANCE AND SCOLIOSIS
A. D. Ruedemann, Jr., Detroit
Discussion to be opened by: William E. Krewson, 3rd, Philadelphia

PITFALLS IN STRABISMUS SURGERY
Walter H. Fink, Minneapolis
Discussion to be opened by: Hermann Burian, Iowa City, Iowa

CAUSES FOR RETINAL DETACHMENT SURGERY FAILURE
Bayard H. Colyer, Jr., and Dohrmann K. Pischel, San Francisco
Discussion to be opened by: Graham Clark, New York

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

6

OCULAR MOTILITY

Rodríguez Barrios, R., and Martínez Recalde, E. **Surgical repair of traumatic inferior rectus palsy.** Arch. oftal. Buenos Aires **30**:311-316, Aug., 1955.

Two cases of traumatic paralysis of the inferior rectus muscle are reported. In the first one a large resection of the affected muscle proved ineffectual, while an intravaginal tenectomy of the reflected portion of the contralateral superior oblique resulted in an almost complete functional cure. In the second, where a large exotropia existed in addition to the vertical disturbance, no traces of the injured muscle could be found at dissection; yet, considerable improvement was achieved by means of transplantation of the whole external rectus muscle and of the lower half of the internal rectus, which were sutured at the place where the scleral insertion of the inferior rectus is normally located. (15 figures, 8 references) A. Urrets-Zavalia, Jr.

7

CONJUNCTIVA, CORNEA, SCLERA

Arkin, W. **Reverse corneal transplant.** Postepy Okulistyki **1**:120-124, 1954.

Experimental autotransplantations were done on rabbit's cornea, with the epithelium inside the anterior chamber. All the transplants grew well but all of them were cloudy. The endothelial surface, placed outside, became epithelized. The epithelium disappeared and the surface of the transplant in the anterior chamber was covered with endothelium. Apparently the epithelium must have an open connection with the outside to become implanted and to spread. There is no advantage in transplanting corneas inside out. (2 figures) Sylvan Brandon.

Bellavia, M. **Vitamin B-12 in high doses in some corneal diseases.** Arch. di ottal. **59**:517-523, Nov.-Dec., 1955.

A solution of 500 micrograms of vitamin B-12 per cc., applied locally, resulted in satisfactory results in six cases of intractable dystrophic or "paradystrophic" conditions of the cornea. (2 references) John J. Stern.

Chavarria Iriarte, Felix-Angel. **Bilateral symmetric perforating scleromalacia.** Arch. Soc. oftal. hispano-am. **15**:1083-1091, Sept., 1955.

A case of bilateral symmetric perforat-

ing scleromalacia is reported in a woman, 50 years of age. She had no rheumatism. A pannus occupied three fourths of each cornea leaving free only the infrainternal quadrant. The literature of this affection is reviewed, and an attempt is made to facilitate by a classification the differential diagnosis. The most important point in the differential diagnosis between scleromalacia perforans and nodular necrosing episcleritis is the absence of pain in scleromalacia, and the presence of pain and inflammatory signs in episcleritis. This affection is included in the group of collagen diseases, and cortisone locally is advocated in the early stages, and intramuscularly if it is associated with rheumatic polyarthritis. Scleroplasty and histiotherapy must be considered in the late stages. (2 figures, 13 references)

Ray K. Daily.

Havener, William H. **Management of conjunctivitis.** Ohio St. M.J. **52**:40-42, Jan., 1956.

Bacterial conjunctivitis will respond to most of the antibiotic eye drops which should be prescribed every one to two hours during the day. Cortisone is indicated in allergic conjunctivitis, but is contraindicated in virus conjunctivitis. Minor irritations respond to nonspecific astringent therapy. Ophthalmic antistine is useful for the watery red eye associated with hay fever. Irwin E. Gaynon.

Renard, G., and Bouzas, A. **The study of corneal diseases by examination with Wood's lamp.** Arch. d'opht. **15**:693-704, 1955.

By means of an ultraviolet lamp (Wood's light), the authors detected corneal fluorescence that appeared 10 to 15 minutes after sclerocorneal incision, continued generally for several days, and disappeared gradually. In some cases the phenomenon persisted longer and the authors consider this persistence a warning of eventual corneal degeneration. They explain the fluorescence as a diffusion of products from the blood into the corneal stroma. They advocate the use of the lamp: 1. in pterygium surgery to determine exactly the margins of the tumor; 2. in major corneal opacities to distinguish between the iris and the lens; and 3. after instillation of fluorescein for the recognition of minimal corneal erosions. They have noted corneal fluorescence in congenital microphthalmos and in leprous subepithelial nodular keratitis. There was no fluorescence noted in cases of corneal anesthesia, in corneal ulcers, after keratoplasty, in glaucoma, in ocular hypotony, or in uveitis. (40 references)

P. Thygeson.

Weigelin, E., and Niessen, V. **The pathologic substrate of the primary bandkeratopathy.** Klin. Monatsbl. f. Augenh. **127**:730-735, 1955.

Two such corneas were available for examination after keratoplasty. In one Bowman's membrane had disappeared and there was a deposition of hyalinelike granula in the superficial stroma. The second cornea had a calcified Bowman's membrane. It is postulated that two types of primary bandkeratopathy exist. (5 figures, 7 references)

Frederick C. Blodi.

8

UVEA, SYMPATHETIC DISEASE AQUEOUS

Hallermann, W. **Diagnosis and treatment of choroidal hemangiomas.** Klin. Monatsbl. f. Augenh. **127**:694-701, 1955.

The 29-year-old woman had poor vision in the right eye since childhood. Adjacent to the disc was a yellowish-red elevation 4 DD long. No pigment could be seen in the retina with the slitlamp. A hemangioma of the skin was found over the right shoulder. Transillumination was

interferred with. Diathermy applications were given about the tumor. When the fundus again became visible (5 weeks after the operation) dense choroidal scars were seen, but part of the elevated tumor was still present. The eye was therefore enucleated and a cavernous hemangioma of the choroid was found. Part of the tumor had been destroyed, but the area closest to the optic nervehead was still viable. (7 figures, 5 references)

Frederick C. Blodi.

Kapuscinski, W. J., and Ogielska, E. **Changes in the aqueous cytology in iritis treated with antistine and typhoid vaccine.** Postepy Okulistyki. 1:67-78, 1954.

The nature and number of cells in the aqueous of 16 patients with iridocyclitis was determined. Three paracenteses were done, one before the treatment, the second after using antistine and the third after the injection of typhoid vaccine. Treatment with antistine usually did not affect the relation of cells. After typhoid vaccine there was a shift of cells toward reticulo-endothelial type and usually clinical improvement of iridocyclitis. (4 figures, 1 table, 13 references)

Sylvan Brandon.

Kapuscinski, W. J., and Wrubel, S. **Influence of alcohol-novocain block of the ciliary ganglion on permeability of the blood-aqueous barrier in uveitis.** Postepy Okulistyki 1:42-57, 1954.

The authors investigated the influence of the nervous system on the inflammatory process by injecting alcohol and novocain into the ciliary ganglion. Permeability of the blood aqueous barrier was examined with fluorescein according to Amsler's method. The results of permeability tests were compared with the clinical influence on the uveitis. In only 11 of 22 patients did the data have similar significance. The authors believe that the influence of alcohol block apparently is beneficial by decreasing permeability of the blood-aqueous barrier, but its effect is limited to the eye. Combining the ciliary block and stimulation by the intravenous injection of typhoid vaccine should be even more effective than either one separately. (3 diagrams, 1 table, 33 references)

Sylvan Brandon.

Neubauer, Hellmut. **Progressive choroidal atrophy.** Arch. f. Ophth. **156**:577-589, 1955.

Neubauer describes a form of central choroidal atrophy which he has been observing for six years in a now 25-year-old woman. Although the clinical manifestations are essentially different from those seen in the other choroidal atrophies, choroideremia and gyrate atrophy of the choroid, all are probably variants of primary disease of choroidal blood vessels.

The segments supplied by the various arterial feeders of the choroid are affected in various combination and extent in the individual types of progressive choroidal atrophy. Whereas in choroideremia and gyrate atrophy the short posterior arteries also take part in producing the atrophy, they alone are the cause of the lesion now described. (7 figures, 20 references)

F. H. Haessler.

Offret, G., and Saraux, H. **Bacteriologic study of human aqueous humor. Technique and results.** Arch. d'opht. **15**:705-731, 1955.

The authors examined 126 specimens of aqueous derived from 113 patients by means of a technique similar to that described by Amsler and Verrey except for an increase in the time of centrifugation. Bacteria were found in both smear and culture in 18 instances, but the aqueous in two of these was from eyes with intraocular foreign body and in four was from eyes with hypopyon ulcer. In three of the remaining 12 cases they were able to identify the bacterium from the aqueous

and one was found in a focus of infection elsewhere in the body.

A definite focus of infection was found in 30 of 54 cases of uveitis. In the series with local infection, microbes were found in 35 percent of the cultures and in 30 to 39 percent of the sediments of centrifugation. Between 10 and 15 percent of the organisms that grew in the cultures were contaminants. In the series without focal infection only 16 percent of the cultures were positive and in these all the organisms seemed to be contaminants. Iridocyclitis after cataract extraction was limited to cases in which extracapsular extraction had been done.

The authors found that rheumatismal uveitis could be separated into two types: 1. true rheumatismal uveitis, which was amicrobic with albumino-cytologic dissociation, and 2. focal infection uveitis in rheumatics. They were unable to isolate tubercle bacilli from so-called tuberculous uveitis. In seven cases of Fuchs' heterochromic cyclitis they found large phagocytes containing bacteria. The authors regard the organisms in uveitis as precipitating factors only and the essential cause as still unknown; hence the relative failure of antibiotic therapy. (10 tables, 98 references) P. Thygeson.

Ogielska, E., Skurski, A., and Ogielski, L. **Color reaction for detection of bacterial toxins in the aqueous in iritis.** Postepy Okulistyki **1**:98-106, 1954.

To determine the presence of bacterial toxins in the aqueous the authors used a colorimetric method based on the fact that methylene blue in combination with silver nitrate, hydrochloric acid and toxins, does not discolor with potassium permanganate. This method is also roughly quantitative. The test showed the presence of bacterial toxins in the aqueous and the conjunctival secretion in acute iritis and iridocyclitis. (4 tables, 3 references) Sylvan Brandon.

Pinero y Carrion, Antonio. **Uveomeningeal syndromes.** Arch. Soc. oftal. hispano-am. **15**:729-814, July-Aug., 1955.

This is the report of the official theme of the Hispano-American Congress, and comprises a comprehensive review of the literature on all phases of the uveomeningeal syndromes, which are the Vogt, Koyanagi and Harada's diseases. 166 cases compiled from the literature are tabulated as to age, sex, involvement of the anterior or posterior uvea, meningismus, associated signs, the Wassermann reaction, general and local symptoms, and the data on the cerebrospinal fluid. Contrary to the prevailing conception, the disease is more frequent among women; 20 percent of the cases were reported from Japan. The average age at the beginning of the disease was 32 years. Meningoencephalitis was present in 58 percent of cases, alopecia in 60 percent, vitiligo in 33.5, poliosis in 50 and disacusia in 43 percent. Anterior uveitis was present in 80 percent of cases, and posterior uveitis in 40 percent. Anterior and posterior uveitis were found in 32 percent. Retinal detachment occurred in 25 percent, and positive signs in the cerebrospinal fluid were found in 80 percent; 37 percent of the patients were left blind; 26 percent could recognize large objects and 63 percent had no useful vision. (27 figures, 3 tables, 226 references) Ray K. Daily.

Samuelly, C. **The importance of the neurovegetative system in the Vogt-Koyanagi-Harada syndrome.** Arch. di ottal. **59**:524-533, Nov.-Dec., 1955.

The author reviews the literature, presents a case, and develops a hypothesis based on the observation that the patient was emotionally unstable. The severe mental trauma which patients with this syndrome undergo may cause disturbances of the vegetative nervous system which lead to secondary disturbances of

the nutrition of the optic disc and generally of the vascular system.

John J. Stern.

9

GLAUCOMA AND OCULAR TENSION

Jabonero, V. **Neurohistologic study of the human ocular tissues after radiation glaucoma.** Acta Neurovegetativa **13**:18-49, 1956.

Histologic changes are described which occurred in an eye in which glaucoma developed after radiation with X rays for carcinoma of the lid. In the cornea there were vacuoles in the vegetative strands in the nervous syncytium. Sensible nerve fibers were completely absent. In the corneal limbus there was severe injury to nerve tissue. In the iris and ciliary body these tissues were normal. (20 figures, 18 references) F. H. Haessler.

Kurimoto, S. **Ocular tension-reducing factor in the spinal fluid of dark-adapted rabbits. I-VI.** Acta Soc. Ophth. Japan **59**: 1854-1880, Dec., 1955.

Kurimoto demonstrated an ocular tension-reducing factor in the spinal fluid of dark-adapted rabbits, the miopiesin of Schmerl. The effect occurs when such fluid is injected intravenously into other rabbits. The reduction of ocular tension thus produced is in the range of 1.0 to 5.0 mm. Hg. The fluid shows no effect on the blood pressure. The results of the fluorescin test suggest that the lowering of tension is brought about by a decreased production of the aqueous. The author further demonstrated that a removal of the superior cervical ganglion impedes the action of miopiesin. He also found that the ocular tension is apt to increase because of dilatation of the pupil when a rabbit is brought in the dark. This increase is, however, compensated in five minutes by an appearance of miopiesin in the system. (5 figures, 3 tables, 157 references) Yukihiko Mitsui.

Ohashi, K. **Influence of chlorpramazine on the experimental elevation and regulation of ocular tension.** Acta Soc. Ophth. Japan **59**:1880-1887, Dec., 1955.

The use of chlorpromazine results in a lowering of ocular tension. An experimental rise of ocular tension brought about by compression of the eyeball, subconjunctival injection of hypertonic saline, low position of the head and compression of the neck is impeded by chlorpromazine. However, the effect of this agent appeared less pronounced in a patient with Horner's syndrome. From these facts Ohashi discusses the bearing of these data on the mechanism of the regulation of the ocular tension. (4 figures, 2 tables, 37 references)

Yukihiko Mitsui.

10

CRYSTALLINE LENS

Leinfelder, P. J., Evans, T. C., and Riley, E. **Production of cataracts in animals.** Radiology **65**:433-438, Sept., 1955.

The authors show that radiation cataract is a real danger, but it can be avoided by the use of proper measures. Progressive changes are less likely to follow exposure to low voltage than to high. Cataract is more probable in those who work with neutrons than in those who are exposed to clinically used X rays. The development of such cataracts exemplifies some of the biologic processes which are provoked by the action of ionizing radiation. (26 references) Irwin E. Gaynon.

Orzalesi, Francesco. **The pathogenesis of complicated cataract.** Ann. di ottal. e clin. ocul. **81**:419-440, Oct., 1955.

The diagnosis of complicated cataract must be based on the presence of other

ocular disturbances and on the typical biomicroscopic findings. Those findings are significant for the interpretation of the pathogenesis.

Cataract is generally regarded as the outcome of a disturbance of the glucoid metabolism of the lens. This theory is not applicable to complicated cataract which must be regarded as the result of changes in the endocular fluids caused by the underlying pathologic condition. The most important change concerns the protein content of these fluids. The author and his group have demonstrated that protein passes through the lens in vitro and in vivo, and that certain protein fractions produce precipitation and opacity of the lens proteins. This mechanism is believed to be active in the pathogenesis of complicated cataract. The protein fractions derive from cell necrosis which accompanies inflammatory, degenerative or dystrophic processes of the inner membranes of the eye. (1 figure, 23 references)

John J. Stern.

Strauss, H., Linn, L., and Ostrow, M. **Electroencephalographic and neuropsychiatric observations in patients with senile cataract.** Mont. Psychiat. u. Neurol. **130**:321-327, Nov., 1955.

Abnormal electroencephalograms occur more frequently in patients with senile cataract than in others of similar age. The authors think it probable that a disorder which they propose to call "lentocerebral degeneration" affects both brain and lens. Patients with an abnormal electroencephalogram often have a severe mental reaction to cataract surgery. (2 figures, 2 tables, 6 references) F. H. Haessler.

11

RETINA AND VITREOUS

Fischer, Franz. **Clinical study of retinitis proliferans in the diabetic.** Arch. f. Ophth. **156**:552-560, 1955.

The author briefly abstracts the contributions which are landmarks in the development of our knowledge of retinitis proliferans in diabetes. A critical survey of this work makes clear its defects: 1. the material of the individual investigator is too small, 2. its relation to the total picture of diabetes is inadequately studied and 3. the general picture of diabetic retinopathy obscures that of retinitis proliferans. Probably the only material that is adequate in all respects is that of H. F. Root of Boston (458 cases in 1952) and it has yielded important concepts.

The author's own material consists of 42 diabetics who have been repeatedly studied in hospital in the course of many years. The onset of the diabetes was most common between 40 and 50 years of age, and not too rarely occurred in patients more than 50 years old. Retinitis usually does not become manifest before the patient's fiftieth year. A long interval between the onset of the diabetes and of retinitis is characteristic and the interval is shorter when the onset of the diabetes occurs later. Hereditary and familial occurrence of the diabetes was manifest to an unsual degree. General arterial hypertension was an almost constant finding and the peripheral form of arteriosclerosis, particularly of the lower extremities, is the commonest. Nephropathy was common but only as part of intercapillary glomerulosclerosis. The retinitis proliferans is a later stage of exudative retinitis. In most of their patients control of the diabetes had been inadequate; strict control as outlined by the Joslin school is a necessity. (55 references)

F. H. Haessler.

Jaeger, W., and Schoenknecht, L. **Statistical study of arterial and venous occlusion in the fundus.** Arch. f. Ophth. **156**:566-576, 1955.

The incidences of these occurrences in

the years 1928 to 1955 were compared with those in the period from 1946 to 1953. It was greatest in 1949 and 1950. The arterial occlusions occurred in branches of the central artery and the venous in the central vein itself. This increase of incidence occurred only in males, not females. In young subjects the prognosis for life is good except when the occlusion is the result of endocarditis, hypertension or an arteriosclerosis that began early. Analysis of the data of the katamnesis did not clarify an otherwise obscure etiology. (4 figures, 3 tables, 18 references) F. H. Haessler.

Kozuchowska, J. **Retinal hemorrhages in newborn.** Postepy Okulistyki 1:167-177, 1954.

Retinal hemorrhages were found in 27 percent of 310 newborn infants within the first few hours after birth. In two-thirds of the infants they were bilateral. (5 figures, 1 table, 15 references)

Sylvan Brandon.

Kraffel, Georg. **Striate chorioretinitis.** Klin. Monatsbl. f. Augenh. 127:664-669, 1955.

A 45-year-old man was observed who developed in both eyes a chorioretinitis which extended in several streaks from the disc into the periphery. (2 figures, 1 table, 11 references)

Frederick C. Blodi.

Lundbaek, Knud. **Diabetic retinopathy in newly diagnosed diabetes mellitus.** Acta Med. Scandinav. 152:53-60, 1955.

Diabetic retinipathy was found in four percent of 246 cases of newly diagnosed diabetes mellitus. All patients were 40 years of age or more. In none of them was the diabetes severe; in two it may have been recent. The author concludes that "diabetic retinopathy in recent diabetes mellitus is of very rare occurrence, if it does occur at all." (1 table, 8 references) Irwin E. Gaynon.

Müller, H. K., Meyer-Schwickerach, G., and Dardenne, U. **Eye manifestations of disturbances of carbohydrate metabolism, with special reference to diabetic retinopathy.** Arq. brasil. de oftal. 17:127-172, 1954.

Diabetes mellitus is the most common and most serious of the anomalies of carbohydrate metabolism, while diabetic retinopathy seems to be increasing in prevalence in spite of advances in the management of the diabetic patient. This long article is a review of statistics of many authors who have studied the retinal probem.

Prior to 1923 retinopathy was not considered as much of a problem, most likely because so many patients died before its onset. The advent of insulin marked a turn in the mortality rate, allowing more diabetics to live longer only to develop retinopathy. Over the years, the frequency of retinopathy has apparently increased from approximately 15 percent in 1923 to about 40 percent in 1953. Some authors have observed it in as many as 62 percent of their diabetics. It is obvious that it is assuming greater importance as a cause of blindness.

Four stages may be observed in the development. The first is the appearance of the well known microaneurysm so well described by Ballantyne and also by Friedenwald. Small intraretinal hemorrhages are also found in this stage. The appearance of waxy exudates marks the second stage. These may be small or moderate in size, or they may coalesce into a large lesion. The posterior pole is most commonly involved, and visual disturbances occur if the macula is affected. Larger hemorrhages may occur. The third stage involves the larger veins which are enlarged and show circumscribed varicosities which resemble a string of pearls. These may be called macroaneurysms. The appearance of new vessels and scar tissue, or retinitis pro-

liferans, marks the fourth stage. This most frequently leads to blindness. All of these stages may be combined with modifications because of arteriosclerosis, hypertension or nephritis. It is emphasized that all of these stages are not continuous, and regression may occur, particularly in the first or second stage.

Current opinion supports the belief that retinopathy is dependent upon the duration of the diabetes. Rare patients have been observed, however, who have been diabetics for 25 years or more who show no signs of retinopathy. It appears to be more common in young males and older females, suggesting the role of a constitutional or hormonal influence. Retinopathy is observed more frequently in those patients with hypertension or arteriosclerosis, but may occur in the absence of either. Increased capillary fragility is also significant, but its role is difficult to assay.

There is close relationship between diabetic retinopathy and intercapillary glomerulosclerosis, the syndrome of Kimmelstiel-Wilson. The histologic picture of the vessels of both conditions is similar, and the two conditions are found in the same patient with great frequency. The appearance of albuminuria, hypertension, edema, glycosuria and retinopathy suggests the presence of the syndrome. Attention is called to the fact that intercapillary glomerulosclerosis is prone to affect the diabetic whose level of blood sugar is comparatively low rather than the individual inclined to acidosis.

Although proof is lacking, there is some circumstantial evidence from numerous authors that other hormones play a role in the genesis of retinopathy. It is postulated that excessive activity or production of pituitary or adrenocortical hormones have an action which opposes that of insulin and thus are somewhat responsible for the retinal disturbance. Clinical observations on women who are in the menopause, or who have become pregnant, and experiments with ACTH and Alloxan have suggested this theory. (7 figures, 10 tables, 131 references)

James W. Brennan.

Nonnenmacher, Heinz. **Heredity and treatment of retinoblastoma.** Klin. Monatsbl. f. Augenh. **127**:735-746, 1955.

This is a review of 30 cases of retinoblastoma observed in Dresden between 1935 and 1954. Eight cases were bilateral. Enucleation of the eye is often followed by X-radiation. Exenteration was necessary in one patient and death occurred soon after the postoperative irradiation.

Two families with retinoblastoma survivors could be followed. Both of them extend over three generations. In one family the affected father had two affected and two normal sons. One normal son had five affected children, two of whom had bilateral tumors. (2 figures)

Frederick C. Blodi.

Sautter, H. **Ateriosclerosis of the fundus.** Klin. Monatsbl. f. Augenh. **127**:641-657, 1955.

In this review article Sautter gives first a short pathologic survey following closely Bell's textbook and Friedenwald.

The clinical picture is divided into four groups: 1. the simple arteriosclerotic fundus with increased arteriolar reflexes and tortuous venules (a tesselated fundus may appear), 2. the dry form of arteriosclerotic chorioretinopathy which is characterized by a decreased permeability of the affected vessels and in which there are pigment changes and cystoid degenerations especially in the periphery, 3. the wet form of arteriosclerotic chorioretinopathy which can be observed when there is an increased permeability of the affected vessels and which leads to hemorrhage, edema, deposits of fat or cholesterol and to macular changes, such as disciform degeneration and 4. the cho-

roidal sclerosis with a yellowish discoloration of the choroidal vessels and pigmentation of the intervascular spaces.

The treatment should include a low-fat diet, raising of the blood pressure (many of these patients have vascular hypotony) and active hyperemia of the retinal vessels. (2 figures, 4 tables, 25 references)

Frederick C. Blodi.

Schenk, H. **Traumatic angiopathy (Purtscher) after ligation of the common carotid.** Klin. Monatsbl. f. Augenh. **127**: 669-676, 1955.

Two patients had a traumatic arteriovenous fistula in the cavernous sinus with pulsating exophthalmus. Whitish grey foci along the veins developed and the veins had in addition numerous constrictions. These changes were seen immediately after the ligation, but not before it. They were of a transient nature and a backflow phenomenon may here be responsible. (3 figures, 16 references)

Frederick C. Blodi.

Seitz, R. **Central serous chorioretinitis.** Klin. Monatsbl. f. Augenh. **127**:676-687, 1955.

Twenty cases were observed during the last two years. During the early stage the subjective symptoms are marked, while the ophthalmoscopic picture may be equivocal. After eight days a round or oval macular elevation appears. A yellow choroidal spot will often appear in the center of this elevation. It may be surrounded by numerous white dots. The retinal vessels remain normal. Micropsia and metamorphosia are common. Paralysis of accommodation is frequent. Fever therapy was usually successful. A focal infection is probably the most important etiologic factor. (12 figures, 2 tables, 15 references) Frederick C. Blodi.

Wasilewski, M. **Retinal and preretinal hemorrhages after blood transfusion.** Postepy Okulistyki **1**:177-184, 1954.

The authors examined 33 patients who had been given 297 transfusions. All but two were examined before the first transfusion and there were 1,400 eyeground examinations. Two patients had hemorrhages before transfusions started, seven developed them after the second transfusion. Among the 12 patients who had hemorrhage, it was preretinal in 11, mixed in two and retinal in one. All of these patients had abnormalities of the blood; seven had pernicious anemia, two leukemia and three secondary anemias. The author feels that the blood pressure is not the factor in the pathogenesis of retinal hemorrhages. (18 references)

Sylvan Brandon.

Wolter, J. Reimer. **Rosettes in a case of advanced retinitis pigmentosa.** Klin. Monatsbl. f. Augenh. **127**:687-694, 1955.

Numerous rosettes were found in both retinas of a 75-year-old man with advanced retinitis pigmentosa. They were found only in dense glial scars. Silver carbonate staining showed that these cylindrical cells have glial processes and may therefore stem from glial and not from neuroepithelial elements. (5 figures, 23 references) Frederick C. Blodi.

13

NEURO-OPHTHALMOLOGY

Abramowicz, I. **Ocular symptoms of intracranial tumors.** Postepy Okulistyki **1**:5-18, 1954.

The importance of ophthalmologists in diagnosing intracranial tumors is stressed. The methods of examination are described and the significance of the diagnostic data are discussed in detail. Increase in the pressure of the central retinal vein is considered significant when the intracranial pressure is elevated. The author lists symptoms and signs appearing in tumors of the frontal lobe, tem-

poral lobe, parietal lobe, occipital lobe, hypophysis and Rathke's pouch, the third ventricle, the corpora quadrigemina and the subtentorial tumors and in meningiomas of the region of the sella turcica and of the small wing of the sphenoid bone. (13 figures, 21 references)

Sylvan Brandon.

Casanovas, Jose. **Pupillotonia.** Arch. Soc. oftal. hispano-am. **15**:1015-1026, Sept., 1955.

Casanovas reports 14 brief case histories of Adie's syndrome; in eight the disturbance was bilateral and in six unilateral. Eight patients were women and six men. Tendon reflexes were absent in ten cases. Two patients had syphilis, and one had a history of hereditary syphilis. One case was associated with a cerebral tumor and one followed fracture of the orbit. Thirteen of the cases were discovered in patients coming for refraction or because of an external disease of the eye. One patient, who had been told that he had Argyll Robertson pupils, came in directly for consultation for this condition. The literature on the evolution, etiology, localization of the lesion, differental diagnosis and treatment is reviewed. (48 references) Ray K. Daily.

Haynes, Phillip R. **A quantitative investigation of the Marcus-Gunn phenomenon.** Am. J. Optometry **32**:621-629, Dec., 1955.

Instead of the usual theory as to the cause of the Marcus-Gunn jaw-winking phenomenon, this author believes it is due to a pseudo-ophthalmoplegia. For it to be due to an aberrant association of the mesencephalic portion of the fifth nerve and the third nerve, the eyelid should stay in the elevated position as long as the jaw is held open. Such an association should also occur in persons without ptosis. The phenomenon could be explained by a lesion in fibers on one side of the brain stem going to the motor nuclei controlling vertical gaze. Such a lesion would remove inhibitory influences from the higher centers, thus exaggerating lower order reflexes. Paul W. Miles.

Henriksson, N. G. **The correlation between the speed of the eye in the slow phase of nystagmus and vestibular stimulus.** Acta oto-laryng. **45**:120-136, March-April, 1955.

A new method for the analysis of the movements of the eye during perrotatory nystagmus is described. The nystagmogram is made by electronically recording the potentials from the lateral angles of the eyes. All recordings are made under carefully standardized conditions. Five observations were made. The speed of the eye in the slow phase varies linearly with the acceleration and the duration of stimulus. The angular speed of the eye in the slow phase equals the rotation of the skull, when the eye is open and uncovered. When the subject is blindfolded the eye speed is less than that of the skull. Eye speed is constant with the stimulus for an individual, but varies from person to person. The speed of the eye is not correlated with the duration of nastagmus when using the same sort of stimulus for cupulometry. (8 figures, 6 tables, 15 references) Harry Horwich.

Lowenstein, Otto. **Pupillary reflex shapes and topical clinical diagnosis.** Neurology **5**:631-644, Sept., 1955.

Eight cases are presented which are representative of the syndromes most commonly encountered in clinical pupillography. Using the infra-red technique, findings were standardized in lesions of the peripheral nervous system; the diencephalon and its connections to the midbrain close to the midline; nonirritative partial lesions of the third nerve nucleus; nuclear or prenuclear irritative lesions of the third nerve nucleus; cen-

tral sympathetic irritation; and parasympathetic or sympathetic weakness. Eighteen topical locations are described. It is the author's opinion that clinical pupillography, which graphically records changes not observable by the unaided eye, aids very materially in the topical diagnosis of these conditions. (9 figures, 5 references) Harry Horwich.

Melanowski, W. H. **New facts in neuro-ophthalmology and their clinical value.** Postepy Okulistyki **1**:19-34, 1954.

The author reviews the anatomy and physiology of the neural components of the eye and of the intracranial visual pathways and centers and describes five patients in whom changes in the visual fields were due to intracranial hemorrhage, tumor or injury. Even small changes, such as difference in the color fields or in the electroencephalogram, may be indicative of a serious intracranial lesion. (16 figures, 15 references) Sylvan Brando.

Unger, Lothar. **Optokinetic nystagmus in psychogenic visual disturbances.** Klin. Monatsbl. f. Augenh. **127**:411-416, 1955.

A 13-year-old girl had a brief hysterical amaurosis during which the optokinetic nystagmus was extinguished. This phenomenon distinguishes this type of hysteria from malingering, where a nystagmus can usually be elicited. (12 references) Frederick C. Blodi.

14

EYEBALL, ORBIT, SINUSES

Albeaux-Fernet, M., and Romani, J. D. **Malignant edematous exophthalmos.** Sem. Hop. Paris **31**:3144-3153, Oct. 14, 1955.

Malignant exophthalmos was recognized by St. Yves in 1722. It occurs more commonly in males and was present in two-thirds of the authors' cases. The edema is not confined to the orbital tissues; pretibial edema is almost constantly demonstrable. The basal metabolism may be elevated, normal or subnormal. This condition most frequently follows hyperthyroidism reduced by surgery, radiotherapy or medication. An interesting suggestion is that the thyrotropic hormone enhances the production of mucopolysaccharides, because of which increased interstitial imbibition in the orbit results. Early cases may be benefited by thyroxine (0.5 to 2 mg. daily), thyroid extract and androgens. In more advanced cases reduction of thyrotropic hormone may sometimes be effected by administration of thymic extract and small doses of iodine. Hypophysial and orbital radiotherapy has an inhibitive action on the pituitary, which lasts however but a few months. The Naffziger operation, unfortunately, is not permanently effective. Recently, various forms of direct surgical attack on the hypophysis have given encouraging results. This comprehensive paper is the seventh contribution by the authors on various phases of this subject. (2 figures, 101 references) James E. Lebensohn.

Boudet, Ch. **The role of the orbital phlebogram in the diagnosis of tumors of the orbit.** Arch. d'opht. **15**:597-618, 1955.

The author comments on the etiologic difficulties encountered in exophthalmos and strongly suggests that orbital phlebography be included among the diagnostic methods. The radiographic study of the orbital veins is accomplished by injecting opaque material into the angular vein. Intraorbital formations are detected by their effect of compressing the veins or of causing deviation of the vessels from their normal course. Finally, pathologic changes in the vessels themselves, as in orbital varices, can be detected. Boudet discusses in some detail the anatomy of the orbit, and particularly the anastomoses of the veins. The article is illustrated by phlebograms of the normal

orbit and of orbits with various types of tumors. Detailed case reports are presented and a bibliography on phlebography is appended. (19 figures, 33 references) P. Thygeson.

Descuns, P., Garré, H., and Aprosio, N. **The two patterns causing traumatic pulsating exophthalmos.** Presse Med. **63**: 1303-1304, Oct. 5, 1955.

Angiography demonstrates that posttraumatic pulsating exophthalmos is not invariably due to simple rupture of the internal carotid into the cavernous sinus, but is determined more frequently by a pre-existing congenital intracavernous aneurysm. The former type requires ligature of the internal and external carotid; the latter needs in addition clipping of the carotid at its exit from the cavernous sinus. Two cases in young women with congenital aneurysm revealed by angiography are presented. (4 figures, 21 references) James E. Lebensohn.

Icken, Ernst. **Hemangio-endothelioma of the orbit.** Klin. Monatsbl. f. Augenh. **127**:472-473, 1955.

A case of recurrent orbital tumor in a 13-year-old boy in reported. Exenteration of the orbit became necessary. The pathologic evaluation was equivocal. (4 figures, 1 reference) Frederick C. Blodi.

Legreze, W. **X-ray radiation to the region of the hypophysis in malignant exophthalmos.** Strahlentherapie. **98**:423-429, 1955.

The incident of malignant exophthalmos has increased, presumably because of increased thyreostatic therapy. Animal experiments have revealed the pathogenetic process which is essentially a disturbance of the functional relationship between thyroid and hypophysis. Thyreostatic therapy results in excessive inhibition of the synthesis of thyroxin which leads to increased production of thyreotropin in the hypophysis which is the cause of the malignant exophthalmos. The hyperproduction can be better controlled by radiation of the region of the hypophysis than by any other therapeutic procedure. It has the additional advantage that radiotherapy of the orbit is included, which has a beneficial effect on orbital inflammation. (19 references) F. H. Haessler.

Lidgett, K., and Wilson, M. M. **Ocular lesions associated with brucellosis. Reports of two cases.** M. J. Australia **2**:900-901, Nov. 26, 1955.

The association of Brucella infection with inflammatory conditions within the orbit is reviewed. Two cases of uveitis probably due to Brucella infection are reported. The authors suggest that in all cases of obscure inflammatory disease within the orbit, serum be titrated by the direct agglutination test and its antiglobulin modification for Brucella antibody. (6 references) Ronald Lowe.

Nataf, R., Besnainou, Reynon, Chantenier, and Spaier. **A case of exophthalmos. Diagnostic difficulties.** Arch. d'opht. **15**: 619-622, 1955.

The authors report the case of a woman of 61 years with left-sided exophthalmos of slow onset and without inflammation but with some pain. The exophthalmos measured 12 mm. and the globe was displaced inferiorly and externally. Motility was markedly restricted, with involvement of the third and sixth nerves. Physical examination revealed an obese, hypertensive, hirsute woman with diabetes and advanced arthritis. Cushing's syndrome was suspected. Radiography of the orbit revealed destruction of the superior internal quadrant of the orbital wall but the nasal sinuses were apparently normal. Surgical intervention disclosed a giant suppurating frontal mucocele with an extraordinary volume of mucopus. The dura

meter was exposed due to bone destruction. The exophthalmos regressed and 13 months later the patient had normal vision, fields, and ocular motility.

P. Thygeson.

Pettinati, Sergio. **Radiographic study of orbital fractures.** Rassegna. ital. d'ottal. **24**:294-320, July-Aug., 1955.

A survey of a very large number of X-ray films showed that 40 percent of them were made for injuries to the orbit. The anatomy and complexity of the structures in this region require that films be made from several angles. Transportation by means of motorcycles and motor scooters in Italy is given as one reason for so many head injuries. Close cooperation between the surgeon and the radiologist is essential. (10 figures, 3 tables, 31 references) Eugene M. Blake.

Schulte, D. **Pseudotumor of the eye and the orbit.** Klin. Monatsbl. f. Augenh. **127**: 385-390, 1955.

A 49-year-old woman had bilateral iritis 15 years ago, 5 years ago a bilateral scleritis and 10 years later bilateral dacryoadenitis which was irradiated four years ago. She came to the clinic with a bilateral exophthalmus (right more than left) and a solid retinal detachment in the left eye. There was a bilateral ptosis and some ocular palsies. A biopsy of the right orbit revealed an unspecific granuloma. Irradiation of the orbit did not prevent progress of the disease and vision is now light perception in the right eye and 5/35 in the left. It is assumed that the inflammatory process of the left orbit also involved the choroid. (5 figures. 4 references)

Frederick C. Blodi.

Shang-Hsien, H., Kung-Choung, A., and Shu-Hsing, A. P. **Granular cell myoblastoma of the orbit.** Chinese M. J. **73**: 437-440, Sept.-Oct., 1955.

A case of granular cell myoblastoma of the orbit is reported. The microscopic characteristics and differential diagnosis are briefly discussed. (2 figures, 14 references) Irwin E. Gaynon.

15

EYELIDS, LACRIMAL APPARATUS

Costi, C. **The results of the first attempts to intubate the naso-lacrimal sac in dacryocystitis.** Arch. Soc. oftal. hispanoam. **14**:1409-1411, 1954.

The tabulated results of 14 cases in which a polyethylene tube was introduced into the naso-lacrimal duct, after the sac was exposed and incised, showed good results in five. The tube was tolerated well in 11 cases, and badly in three. In these three the sac was finally extirpated. Permeability was restored in five cases, the sac was permeable with difficulty in five cases, and the obstruction remained complete in four cases. In the five patients in whom of permeability was difficult it was restored with several probings. There was no epiphora in seven cases, and in seven cases it continued. (1 table) Ray K. Daily.

Frezotti, Renato. **Epidemiology of palpebral leishmaniasis.** Gior. ital oftal. **8**: 312-321, July-Aug., 1955.

A patient with a leishmania lesion in the medial third of the upper lid is described. It is associated epidemiologically with cutaneous leishmaniasis described by Agostini and others in the province of Siena and Grosseto. Treatment by the systemic administration of a preparation of antimony was successful; no local treatment was applied. (2 figures, 15 references) V. Tabone.

Juge, P. **Dacryocystorhinostomy: technique of attaching the lacrimal sac in the nasal fossa.** Arch. d'opht. **15**:732-735, 1955.

The author reviews the technique of dacryocystorhinostomy and notes that one of the difficult features of the operation is the suturing of the sac to the nasal mucosa. The sutures have a tendency to cut out with resultant malposition. Failure of the operation is believed in many instances to result from the canalicular orifice's being too near the upper edge of the bony opening. The author proposes a surgical modification that involves the utilization of the entire sac. The sac is cut loose from the nasolacrimal duct and the cut end is attached by four sutures to a circular orifice in the nasal mucosa, 3 to 4 mm. wide and in the center of the bony opening. The sutures are placed, one posteriorly, two laterally, and one anteriorly. If the sac is too long, its length is adjusted by scissors to an optimum. No folds or traction lines should occur. The results of this procedure have been satisfactory. (3 figures) P. Thygeson.

Mietke, Hans. **Cytomegaly of the lacrimal gland.** Klin. Monatsbl. f. Augenh. **127**:400-403, 1955.

Cytomegaly is a virus disease which is characterized by the appearance of large, unilocular cells in glands (especially salivary glands) and the parenchymatous organs. These cells contain inclusion bodies. This 59-year-old woman had recurrent orbital tumors on one side. The appearance of the characteristic large cells in the cirrhotic lacrimal gland revealed the diagnosis. (2 figures, 8 references)
Frederick C. Blodi.

Orbán, Tibor. **A papillary, proliferating cystadenoma of Moll's glands.** Klin. Monatsbl. f. Augenh. **127**:473-477, 1955.

Histologically, a recurrent tumor in the upper lid of a 77-year-old man proved to be a cyst-like tumor of a sweat gland. (6 figures, 12 references)
Frederick C. Blodi.

la Rocca, Vito. **Retraction of the upper lid after enucleation.** Gior. ital. oftal. **8**: 356-359, July-Aug., 1955.

A case of retraction of the upper lid following enucleation is described; treatment was successful by means of a fascia lata graft. The technique used is described. (4 figures, 2 references)
V. Tabone.

Strampelli, B. **A practical modification of the method of Cattaneo for the correction of ptosis.** Boll. d'ocul. **34**:395-402, July, 1955.

The author describes a ptosis operation in which a band of orbicularis muscle is hooked around a previously outlined button of skin at the midpoint of the brow line. He states that the final result has been excellent in the 12 patients on whom he has performed this operation. (6 figures) William C. Caccamise.

16

TUMORS

Maddock, W. G. and Lien, R. M. **Calcified liver nodules from metastatic primary melanoma; ocular primary fifteen years previously.** Northwestern Univ. Med. Sch. Quart. Bull. **29**:374-379, 1955.

This patient had an enucleation performed for melanoma 15 years ago. Five years after the onset axillary metastases were removed. Now he has metastases in the liver. Roentgenographic examination of the liver revealed multiple calcified areas. At surgery, the metastases were found to be encapsulated by a dense collagenous capsule and calcium salts, indicating an unusual degree of resistance to tumor growth. The patient is alive and working at his occupaton. (2 figures, 21 references) Irwin E. Gaynon.

Negri, L., and Rizzini, V. **Biological aspects of malignant melanomas of the**

uvea. Gior. ital oftal. **8**:292-311, July-Aug., 1955.

Material obtained from 15 cases of melanoma of the uvea was studied histochemically. Details of cases are given as well as details of coloration. The following substances were particularly studied: 1. glycogen, 2. nucleic acids, and 3. lipoids and other substances staining with Sudan III. Glycogen was found in variable but often considerable quantities; different methods of coloration gave different figures for nucleic acids. The great prevalence of cells of type A according to Casperson, is stressed. Substances taking Sudan III coloration were usually abundant in the cytoplasm of cells, mostly in the form of fine granules. The importance of the findings in relation to the prognosis is discussed. (7 figures, 38 references)

V. Tabone.

Trzcinska-Dabrowska, Z. **Melanoma of the eye.** Postepy Okulistyki **1**:184-197, 1954.

The author reviews classification, etiology and pathogenesis of melanomas. Their origin from the neuroepithelium is accepted. The clinical course of a melanoma is described including the methods of diagnosis. The experience in 46 cases is described; 34 of them originated in the choroid, five in the conjunctiva, three in the ciliary body, one in the iris and in the lid and in two the origin was uncertain. Microscopically there were 18 tumors of mixed cell origin, 14 epitheloid, 13 fusiform A and 1 fusiform B. The melanomas appeared most frequently in the fifth decade of life, they were fairly large because of late examination; detachment of the retina and glaucoma were frequent. Prognostically epithelioid cells were a sign of malignancy whereas the presence of reticulum suggested a more benign course. (12 figures, 16 references)

Sylvan Brandon.

17
INJURIES

la Rocca, Vito. **Argyrosis of the anterior sector of the eye.** Gior. ital. oftal **8**: 352-355, July, Aug., 1955.

A patient is described in whom there was chronic argyrosis of the nails, the conjunctiva, the cornea and the lens. The man had been exposed to silver salts for 43 years. The cataractous lens was removed successfully, but the patient died two years later with tumor of the liver. The possible association of this tumor with deposition of silver in the liver, as well as some medicolegal aspects of complicated cataract, are discussed. (3 figures, 6 references. V. Tabone.

Schoenewald, H. K. **Extraction of a piece of glass from the chamber angle.** Klin. Monastbl. f. Augenh. **127**:596-600, 1955.

A 12-year-old girl was injured when a bottle exploded. The left eye remained irritated for 10 months. The piece of glass was visible with the gonioscope and could be extracted with a cataract forceps. (32 references) Frederick C. Blodi.

Zintz, R. **Traumatic damage to the chiasm.** Klin. Monatsbl. f. Augenh. **127**: 539-546, 1955.

Injuries of the chiasm are rare and occur with fractures of the skull. They are not caused by boney fragments injuring the chiasm but by a sagittal tear through that structure (Coppez). It occurs when a severe blow hits the occipital or frontal area. One case was seen (21-year-old man, motorcycle injury) where the typical bitemporal hemianopia followed. In another patient, however (49-year-old man, fall from tractor), a binasal hemianopia developed. It must be assumed that in this case the small vessels from the carotid artery to the chiasm were ruptured. (4 figures, 34 references)

Frederick C. Blodi.

18

SYSTEMIC DISEASE AND PARASITES

Buesa, Lorente. **Ocular filariosis.** Arch. Soc. oftal. hispano-am. **14**:1417-1422, Dec., 1954.

The author reports a case of filariosis of the conjunctiva in a woman who resided for a year in Spanish Guinea. After living there for six months she was bitten in the foot by an insect; the bite produced an irritation which lasted one year. Some time later she noticed a thread in her left eye, which when extracted by the author proved to be a Filaria Loa. After the extraction the patient had blood studies, which were negative for the parasite, and for the two and one half years after the extraction she had no further symptoms. (3 figures, 5 references) Ray K. Daily.

Kato, K., Abe, Y., and Suzuki, S. **Ocular symptoms and blood pressure of the central retinal artery with heart diseases.** Acta Soc. Ophth. Japan **59**:1364-1370. Sept., 1955.

Ocular findings, with special reference to the retinal blood pressure in 69 patients with anomalies of the heart, are described. A congestion of conjunctiva and retina in two patients and a retinal thrombosis in one were the only ocular manifestations ascribed to anomalies of the heart. However, anomalous blood pressure in the central artery of the retina was common. The diastolic retinal pressure was low in aortic stenosis and mitral stenoinsufficiency. It was high in patients with tetralogy of Fallot. In a patient with a persistent Botallo's duct, retinal systolic pressure was high. With mitral insufficiency there was a lowering of retinal diastolic pressure and the proportionately more lowering was higher than in the radial artery. A similar relationship was observed in the systolic pressures of mitral-stenoinsufficiency.

The authors further describe the improvement in the anomalous retinal blood pressure after heart surgery. (6 tables) Yukihiko Mitsui.

Lee, F. M. **Ocular manifestations in xeroderma pigmentosum with report of three cases.** Chinese M. J. **73**:429-435, Sept.-Oct., 1955.

Three cases of xeroderma pigmentosum with ocular manifestations are described. All the patients were girls from 8 to 12 years of age. One of them had a family history of consanguineous marriage. The skin lesion developed quite early in life. Both the ocular and skin manifestations were marked. The symptoms improved after radiotherapy. The patients in cases two and three were sisters. Their ocular manifestations and clinical symptoms were very similar. (9 figures, 11 references) Irwin E. Gaynon.

Leipert, Gotthard. **Fatty aqueous and temporary hyperlipemia in Sheehan's syndrome.** Klin. Monatsbl. f. Augenh. **127**: 558-565, 1955.

Sheehan's syndrome is a postpartum hypopituitarism caused by a vascular atrophy of the hypophysis. The secondary hypothyroidism may lead to hyperlipemia. A 34-year-old woman had her last delivery 13 years ago. Since then she felt weak, had chills, myxedema, lost her hair, and xanthomas developed on the skin. She came to the clinic because of a cyclitis in the right eye. The aqueous in that eye was milky and contained about 10 percent fat. There was a lipemia of the retinal vessels and the total fat in the serum was 4.4 percent. There were also lipoid deposits in the cornea. The condition improved on fat-free diet. (1 figure, 4 tables, 22 references) Frederick C. Blodi.

Mata Lopez, Pedro. **Rheumatic ocular diseases.** Arch. Soc. oftal. hispano-am. **15**: 1039-1053, Sept., 1955.

The literature on the modern conception of the rheumatic ocular syndromes, which may be adaptation syndromes or collagenous diseases, is reviewed. The diagnostic difficulties of rheumatic diseases limited to the eye are pointed out, and two illustrative cases briefly reported. One patient had a resistant monocular nodular episcleritis and the other an acute monocular tenonitis. A year later one patient developed a chronic polyarthritis, and the other an articular osteoarthritis. A case of embolism of the central retinal artery in a patient, 22 years old, with acute rheumatic endocarditis is reported to illustrate the possibility of ocular complications in cases of cardiac rheumatic disease. That chronic arthritis may be associated with ocular lesions of nonrheumatic etiology is illustrated by the report of chronic arthritis and acute uveitis in a woman 35 years of age. After a tonsillectomy and the removal of buccal sepsis, the uveitis cleared, but the rheumatic condition persisted unimproved. The subject is divided into sections on idiopathic and secondary rheumatic ocular lesions, the localization of lesions in the various segments of the globe and in the vascular tunic, diagnosis, and treatment. (43 references)

Ray K. Daily.

Sasamoto, M. **Relation of acetylcholine test with blood pressure and fundus finding in hypertensive patients.** Acta Soc. Ophth. Japan **59**:1371-1382. Sept., 1955.

Sasamoto studied the acetylcholine test in hypertensive patients. One observes an erythema caused by an injection of the agent for 90 minutes. In normal man, the reaction is strong and the duration of the positive reaction is over 75 minutes. In hypertensive patients, there is a reduction in the intensity and duration of the reaction parallel to an advance in the fundus change, and an increase in the diastolic blood pressure of the body. In the stage IV of hypertension by Keith-Wagener, the reaction is the lowest in general and the duration is less than 60 minutes.

The author believes that the test gives an indication of the functional state of the artery and, therefore, a basis for judgement of prognosis in hypertensive patients. The Keith-Wagener classification provides evaluation of the anatomic stage of the hypertension and the present test of a functional stage. (5 figures, 8 tables, 33 references)

Yukihiko Mitsui.

Takahashi, M. **Anoxia in the central nervous system, particularly in the visual pathway, caused by pitressin.** Acta Soc. Ophth. Japan **59**:1388-1397. Sept., 1955.

This is a study of the changes in the central nervous system caused by repeated pitressin (vasopressin) injections in rabbits. The agent was given intravenously, four units per Kg. body weight as one injection, for four times in one day. Clinically, an atrophy of the optic nerve began to appear about one month after the injection. An ataxia appeared two weeks later. Mydriasis and disappearance of light reflex became apparent meantime. Histologically, Takahashi was able to demonstrate a demyelinating process in the central nervous system following a vessel contraction and thrombus formation. He considers the experiment an aid in the explanation of the developmental mechanism of multiple sclerosis and like conditions. (18 figures, 1 table, 19 references)

Yukihiko Mitsui.

Trias De Bes, L., Sanches Lucas, J. G., and Ballesta Barcons, F. **A case of Takayashu's syndrome: the pulseless disease.** Brit. Heart J. **17**:484-488, Oct., 1955.

A case of pulseless disease in a 19-year-old woman is described. No pulsation could be felt in the carotid, axillary, brachial or radial arteries. In the right eye there was a complete cataract, pos-

terior synechiae, iris atrophy, and a malignant secondary glaucoma that later made it necessary to enucleate the eye. In the left eye there were some peripheral opacities of the lens, filaments and floating bodies in the vitreous, and early primary optic atrophy. The retina was yellowish, its veins were markedly enlarged, the blood flow was irregular and in color like coffee grounds. A large arteriovenous anastomosis was seen in the temporal portion of the retina. Vision in the left eye was 1/10. Examination of the enucleated eye revealed mesenchymal anomalies which suggest a possible congenital basis for the disease. (4 figures, 7 references) Irwin E. Gaynon.

Venturi, G. **Temporal arteritis (case report).** Arch. di ottal. **59**:453-488, Nov.-Dec., 1955.

The author presents an extensive review of the literature and a detailed report of a case of temporal arteritis. (72 references) John J. Stern.

19

CONGENITAL DEFORMITIES, HEREDITY

Goslich, Hildburg. **Clinical and electroretinographic examinations of three generations of familial hereditary juvenile macular degeneration.** Klin. Monatsbl. f. Augenh. **127**:657-663, 1955.

Four members of a family with the Stargardt type of macular degeneration could be examined. The central vision was poor even in the youngest member. The ERG, however, was normal in all patients, except for a slight depression of the b-wave in the oldest member (62-year-old man). This is another proof that this type of tapetoretinal degeneration affects the cones only. (4 figures, 32 references) Frederick C. Blodi.

Leuenberger, Adolf. **Congenital microphthalmus and other malformations of the visual organ.** Arch. f. Ophth. **156**:162-176, 1955.

A prematurely born girl who died four days after birth showed the following malformations: bilateral absence of lens, iris, ciliary body and cornea. Well developed and vascularized connective tissue and retinal folds extending into the space of the vitreous body resembled a coloboma. In the left eye a hyaloid artery persisted. The malformation probably belongs into the group of retinal dysplasias. (4 figures, 25 references)

* Ernst Schmerl.

la Rocca, Vito. **Atypical coloboma of the choroid and of the optic disc.** Gior. ital. oftal. **8**:348-351, July-Aug., 1955.

A patient is described in whom there was a partial coloboma of the optic disc and of the choroid in one eye, and a pseudopapillitis in the other. This patient had a cavernous angioma of the face in childhood, a datum which supports the theory of Collins that the vascular etiology of colobomas is acceptable. (1 figure, 7 references) V. Tabone.

Urrets-Zavalia, Jr., Alberto. **Familial primary hypoplasia of the orbital margin.** Tr. Am. Acad. Ophth. **59**:42-59, Jan., 1955.

The author describes the pedigrees of two identically affected families with craniofacial dysostosis. Characteristics of this rare disorder of high familial incidence are marked agenesia of the orbital margin, polymorphic lacrimal anomalies and aplasia of tarsal plates and skin of lids. The condition is transmitted as a dominant character. (8 figures, 45 references) Theodore M. Shapira.

Vannini, Angelo. **Gonioscopy in congenital cataracts.** Rassegna ital. d'ottal. **24**:281-284, July-Aug., 1955.

Many eyes with congenital cataract show mesodermal tissue in the angle of the anterior chamber and fetal defects

in other structures of the globe. Such alterations often indicate the period of development when the anomalies arose. Three cases are illustrated. In one case mesodermal tissue covers the ciliary muscle and scleral trabeculae, the second shows insertion of the iris on the corneal wall, while in the third the iridocorneal angle is occupied by abnormal uveal trabeculae. (3 figures in color, 4 references)

Eugene M. Blake.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Viel, Benjamin, et al. **The ophthalmologic problems of the school children in Santiago.** Arch. chil. de oftal. **12**:69-74, Jan.-June, 1955.

The authors have examined several thousands of school children in Santiago and believe that, for lack of specialists and nurses, a routine eye examination should not be part of the regular school examination. They found few abnormalities during their survey, but do recommend that visual acuities be tested periodically by someone in the school. Only those children who have low acuity should be referred for further examination. (3 tables)

Walter Mayer.

Watkins-Pitchford, D. **The assessment of eye injuries in industry.** Tr. Ophth. Soc. U. Kingdom **74**:523-525, 1954.

As the minister of National Insurance, the author gives a short account of the National Insurance Act of 1948, which insures (a) all persons against personal injury by accident provided the injury arises out of and in course of insurable employment and (b) persons ill with certain diseases known as prescribed diseases provided that the insured person is in the related occupation at the time of onset.

Beulah Cushman.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 12th of the month. For adequate publicity, notices of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Joseph Stanton Hory, New York, New York, died January 1, 1956, aged 60 years.

Dr. Tom Otto W. Meissner, Athens, Georgia, died September 29, 1955, aged 44 years.

Dr. Samuel Archard Morris, Los Angeles, California, died December 3, 1955, aged 51 years.

Dr. George Waverly Nairn, Warsaw, New York, died October 28, 1955, aged 60 years.

Dr. Peter Hunter Thompson, Boston, Massachusetts, died December 1, 1955, aged 82 years.

ANNOUNCEMENTS

ORTHOPTIC COURSE OFFERED

The Kresge Eye Institute again offers its facilities for the training of orthoptic technicians. This program is open to any young woman over 20 years of age, who has successfully completed at least two years of college or is a graduate nurse. Good health and vision are required of the trainees.

The course consists of 12 months' didactic and practical training. Didactic training, which is part of the basic ophthalmology course for doctors at Wayne University Graduate College of Medicine, will be given five mornings a week for the first semester. Lectures on refraction, retinoscopy, physiological optics, perimetry, ocular anatomy, neuroanatomy, and motility are given by members of the Kresge Eye Institute staff and professors of Wayne University College of Medicine.

Practical training must begin in mid-August, one month prior to the beginning of the lecture courses. This practical training continues for one year, at which time students are eligible to take the board examinations for certification given by the American Orthoptic Council orally in August and in writing each fall.

Limited financial assistance is available for some students who require it. Requests may be made either through Kresge Eye Institute or the Delta Gamma Fraternity (Mrs. H. V. Draheim, 19641 Coral Gables, Birmingham, Michigan.)

For further information write to:

A. D. Ruedemann, M.D.
Kresge Eye Institute
690 Mullett Street
Detroit 26, Michigan

ACTA XVII CONGRESS

Acta XVII Concilium Ophthalmologicum 1954 (Canada-United States of America), the official publication of the XVII International Congress of Ophthalmology has been distributed to full members and advance subscribers. A limited number of sets (three volumes) are still available. Price: $20.00 postpaid. Send orders and remittance to:

W. L. Benedict, M.D., Secretary-General
100 First Avenue Building
Rochester, Minnesota

HOME STUDY COURSES

The 1956-1957 Home Study courses in the basic sciences related to ophthalmology and otolaryngology, which are offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1, 1956, and continue for a period of 10 months. Detailed information and application forms can be obtained from:

Dr. William L. Benedict,
Executive Secretary-Treasurer
100 First Avenue Building,
Rochester, Minnesota

Registrations should be completed before August 15, 1956.

ORTHOPTIC EXAMINATIONS

The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in August and October, 1956.

The written examination will be nonassembled and will take place on Thursday, August 23, in certain designated cities and will be proctored by assigned ophthalmologists.

The oral and practical examinations will be held on Saturday, October 13, in Chicago just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Application for examination will be received by the office of the Chairman of Examinations:

Dr. Frank D. Costenbader
1605 22nd St., N.W.
Washington 8, D.C.

Applications, which must be accompanied by the examination fee of $30.00, will not be accepted after July 1, 1956.

SOCIETIES

WILMER MEETING

The 15th clinical meeting of the Residents Association of the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital and University, was held in Baltimore April 19-21.

PITTSBURGH MEETING

On the ophthalmology program of the joint meeting of the Pittsburgh Ophthalmological Society and the Pittsburgh Otological Society with the South-

western Pennsylvania chapter of the American College of Surgeons held recently in Pittsburgh were:

Medical motion pictures: (Dr. Jay G. Linn, Jr., presiding):

"Corneal transplantation for endothelial and epithelial dystrophy (Fuchs)," "Cataract extraction: The technique of zonule stripping," "Cataract extraction by inferior approach after filtering operation for glaucoma," "Cataract with glaucoma," "Extraction of cataractous lens after filtering glaucoma operation," and "Mechanical forces in intracapsular cataract extraction."

Dr. Thomas C. McLellan presided over the Symposium on retinal detachment:

"General considerations and classification of detachment of the retina," Dr. Graham Clark, New York; "Examination of the patient: Using direct and indirect ophthalmoscopy, as well as the slitlamp examination of the vitreous," Dr. Harvey E. Thorpe, Pittsburgh; "The diathermy operation: Objective, methods and currents," Dr. Clark; "The scleral folding operation: Indications, advantages over other scleral shortening operations, and techniques," Dr. William G. Everett; "Postoperative care," Dr. Clark.

Symposia on preoperative and postoperative care and on auto injuries were also presented.

Puget Sound Academy officers

Officers of the Puget Sound Academy of Ophthalmology and Otolaryngology are: President, Dr. Russell T. Horsfield; president elect, Dr. A. George Hanson; secretary-treasurer, Dr. Willard F. Goff; trustees, Dr. R. T. Horsfield, Dr. A. G. Hanson, Dr. W. F. Goff, Dr. W. C. Cameron, Dr. J. A. Weber, Dr. E. D. Anderson, and Dr. C. D. F. Jensen.

Los Angeles society

The Los Angeles Society of Ophthalmology and Otolaryngology meets at the Los Angeles County Medical Association Building, 1925 Wilshire Boulevard, Los Angeles, at 6:00 P.M., on the fourth Monday of each month (otolaryngology section) and the first Thursday of each month (ophthalmology section) from September to June, inclusive.

Officers for the society are: President, Dr. Leland R. House; secretary-treasurer, Dr. Sol Rome; chairman ophthalmology, Dr. Stephen J. Popovich; secretary ophthalmology, Dr. Richard Kratz; chairman otolaryngology, Dr. Harold Boyd; secretary otolaryngology, Dr. Howard G. Gottschalk.

Richmond (Virginia) society

The Richmond (Virginia) Eye, Ear, Nose and Throat Society meets the first Tuesday of May and October at the Commonwealth Club. Officers of the society are: President, Dr. Ed Bryce; secretary-treasurer, Dr. Charles N. Romaine.

Brooklyn meeting

At the 137th regular meeting of the Brooklyn Ophthalmological Society, Dr. Harold Whaley Brown spoke on "Convergence insufficiency," and Dr. J. Arnold DeVeer discussed "Conjunctival nevi."

Personals

Dr. Frederick C. Blodi, Iowa City, Iowa, has been elected to honorary membership in the Kansas City Society of Ophthalmology and Otolaryngology.

Presentation of Sir Stewart Duke-Elder's portrait (painted by Ruskin Spear, R.A.) jointly by The Faculty of Ophthalmologists and The Ophthalmological Society of the United Kingdom took place on April 26, at the Royal College of Surgeons, Lincoln's Inn Fields, London.

Dr. Arthur J. Bedell, Albany, New York, has been elected the first honorary member of the Ophthalmological Society of South Africa.

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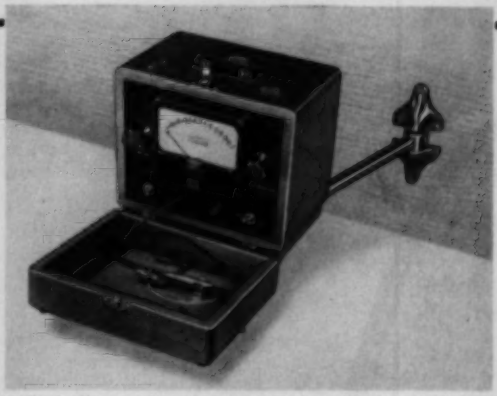

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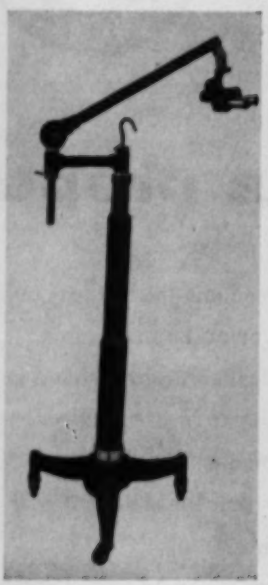

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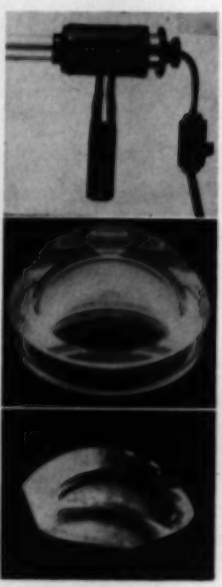

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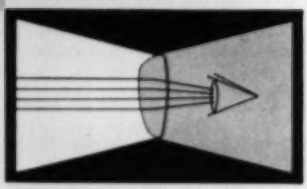

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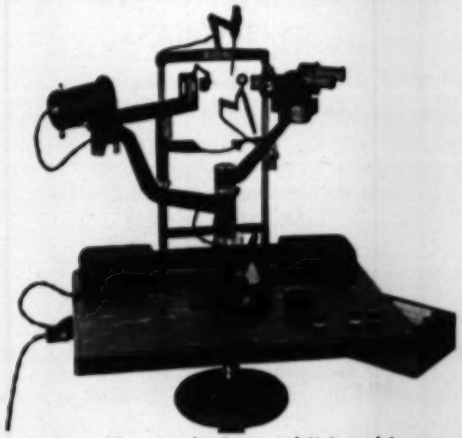

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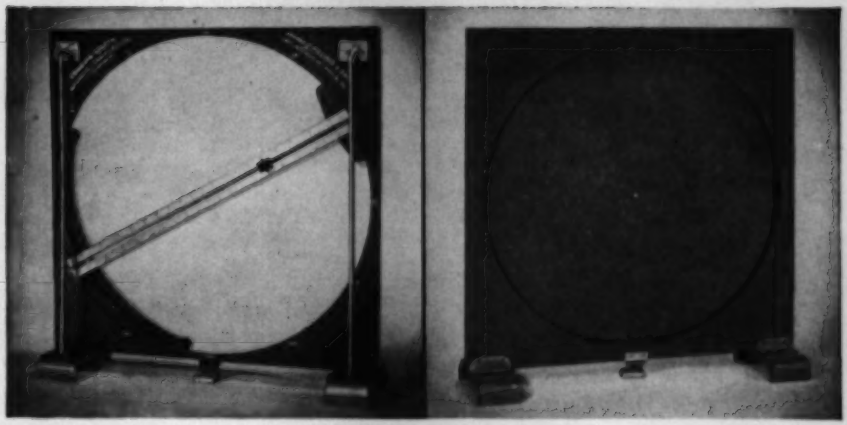

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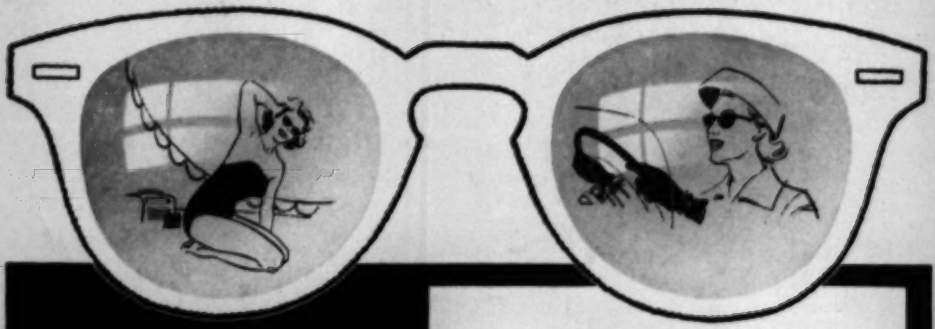

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